UNIVERSITY OF MICHIGAN
OCT 24 1950
MEDICAL LIBRARY

Volume XI OCTOBER 1950 Number 10

DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

CONTENTS:

THE ASSOCIATIVE ANAMNESIS IN TEACHING INSIGHT PSYCHOTHERAPY 291
William F. Murphy, M.D., and Sidney Kligerman, M.D.

EVALUATION OF RESULTS FROM LEUKOTOMY IN SCHIZOPHRENIA 298
Myron Feld, M.D.

NON-CONVULSIVE ELECTRO-STIMULATION IN INSULIN COMA 302
Francis H. Hoffman, M.D., and Charles A. Wunsch, M.D.

UNUSUAL MENTAL SYMPTOMS IN A CASE OF HEPATOLENTICULAR DEGENERATION 305
W. M. Gysin, M.D., and Edwin T. Cooke, M.D.

NEUROLOGICAL CLINICAL PATHOLOGICAL CONFERENCE 310

SANITARIA

ASSOCIATE EDITORS

A. E. Bennett, M.D. ..... Berkeley, California
Francis J. Braceland, M.D. ..... Rochester, Minn.
Franklin G. Ebaugh, M.D. ..... Denver, Colorado
Temple Fay, M.D. ..... Philadelphia, Pennsylvania
Milton H. Erickson, M.D. ..... Phoenix, Arizona
Hamilton Ford, M.D. ..... Galveston, Texas
Walter Freeman, M.D. ..... Washington, D.C.
George T. Harding, M.D. ..... Columbus, Ohio
A. Hauser, M.D. ..... Houston, Texas
Louis J. Karnosh, M.D. ..... Cleveland, Ohio
Frank H. Luton, M.D. ..... Nashville, Tennessee
Wm. Malamud, M.D. ..... Boston, Mass.
Karl A. Menninger, M.D. ..... Topeka, Kansas
Hans H. Reese, M.D. ..... Madison, Wisconsin
S. Bernard Wortis, M.D. ..... New York, N. Y.

Titus H. Harris, M.D.
Galveston, Texas
Editor-in-Chief

YEARLY SUBSCRIPTION $4.00
SINGLE COPIES 40 Cents
FOREIGN SUBSCRIPTION $4.50

George Bisgeir, B.S., LL.B.
Chicago, Illinois
Managing Editor

THE RING SANATORIUM

Arlington Massachusetts

Eight miles from Boston at an elevation of 400 feet

72nd Year

For the study, care and treatment of emotional and personality disorders.
All recognized psychiatric therapies as indicated.

Cottage accommodations meet varied individual needs. Limited facilities for the continued care of progressive disorders requiring medical, psychiatric or neurological supervision.

BENJAMIN SIMON, M.D.
Director

CHARLES E. WHITE, M.D., LOUIS BRENNER, M.D.
FRED E. LAWRENCE, M.D.
Associates

HARDING SANITARIUM

WORTHINGTON, OHIO

For Nervous and Mental Disorders

NINE MILES NORTH OF STATE HOUSE — COLUMBUS

HARRISON S. EVANS, M.D., Medical Director
GEORGE T. HARDING, M.D., President of Board
CHARLES L. ANDERSON, M.D., Clinical Director

L. HAROLD CAVINESS, M.D.
J. RUSSELL FRANTZ, M.D.
THEODORE J. LUKENS, M.D.
LESLIE H. GOULD, M.D.
CHARLES W. HARDING, M.D.

Telephone: Columbus FR. 2-5367

Compton Sanitarium

AND

Las Campanas Hospital

COMPTON, CALIFORNIA
(Near Los Angeles)

Compton Sanitarium is a private psychiatric hospital with 120 beds. Emphasis is given psychotherapy by a staff of resident psychiatrists. Other treatment procedures are duly evaluated and administered. Careful records are maintained. There are psychiatrically trained graduate nurses; student nurses through affiliation; nursing attendants; dietitian; occupational therapist; recreational therapist; hydrotherapist; masseuse. Las Campanas Hospital (43 beds) provides adjunct general hospital facilities. Compton Sanitarium and Las Campanas Hospital are approved by the American College of Surgeons.

G. CRESWELL BURNS, M.D., *Medical Director.*

BEVERLY HILLS CLINIC and SANITARIUM

For the Study and Treatment of Nervous and Mental Diseases

218 NO. WESTMORELAND DALLAS 11, TEXAS

This sanitarium is a psychopathic hospital with a home-like environment and is equipped to treat psychiatric and neurological cases in a most scientific manner by means of psychotherapy, occupational therapy, recreational therapy, and physiotherapy, including insulin and electroshock treatments as well as neurosurgery. There is a trained psychologist as well as a trained social worker. An electroencephalographic instrument is available.

ARTHUR J. SCHWENKENBERG, M.D.
Medical Director

JOSEPH L. KNAPP, M.D.
Associate Psychiatrist and Clinical Director

JOHN C. POWELL, JR., M.D.
Associate Psychiatrist

ARCHIE R. FOLEY, M.D.
Senior Resident Psychiatrist

STEPHEN WEISZ, M.D.
ROBERT R. WINN, M.D.
Visiting Neuropsychiatrists

VOL. XI OCTOBER 1950 No. 10

Published monthly by
PHYSICIANS POSTGRADUATE PRESS
277 Broadway, New York 7, New York

EDITORIAL OFFICES
UNIVERSITY OF TEXAS SCHOOL OF MEDICINE
800 Avenue B., Galveston, Texas

Entered as second-class matter at the Post Office at New York, N. Y.

DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

The Associative Anamnesis in Teaching Insight Psychotherapy

WILLIAM F. MURPHY, M.D.,* and
SIDNEY KLIGERMAN, M.D.**
Framingham, Massachusetts

Introduction

This paper is concerned with our experiences in teaching psychiatric residents a practical method of applying the principles of insight psychotherapy during the six months they spend on the Open Ward Service at Cushing V. A. Hospital where non-psychotic and psychosomatic cases are treated.

At the beginning of the teaching program, we tended to rely primarily on tutorial case supervision and clinical conferences. We took it for granted that the residents had or would soon develop sufficient familiarity with the associative techniques of interviewing and the principle of minimal interference that is such an essential part of these techniques. It was expected that ultimately, through trial and error and imitation of the supervising psychiatrist, the residents would realize that question-answer techniques and the use of personal charm eventually defeat their own purpose. In this belief we were over-optimistic inasmuch as we found that at the end of a six to nine month period the residents, apart from an exceptionally gifted few, tended to pay only lip service to dynamic concepts. It was found that (1) Most of the residents had great difficulty in detecting the unconscious motivations of the patient's symptoms. Consequently the role they played in the patient-doctor relationship and the connection between the present patterns of behavior and the ones utilized in infancy were seen only in the most superficial aspects. (2) A number of problems arose based on the personality difficulties of the individual resident, many of which have been discussed in a previous paper.[1] (3) The residents tended to rely too much on intuition before their experience with patients and their understanding of their own emotional problems made this intuition reliable.

It soon became apparent that most of these difficulties arose from the fact that we were unable to bridge the gap between what went on during the patient-resident interviews and what the resident reported to the supervising psychiatrist. Teaching during tutorial sessions had been made difficult by the vagueness of the case reports and the difficulty on the part of the residents in giving concrete examples. Early in 1948 we installed microphones in the resident psychiatrist offices and began making direct recordings of the doctor-patient interviews. When recorded interviews became available for discussion, they revealed to both residents and supervising psychiatrists that the patient was telling the doctor much that was being missed by him. They revealed some of the reasons for the previously mentioned difficulties and the vagueness of the reports.

*Chief, Open Ward NP Service.
**Asst. Chief, Open Ward NP Service.
From the Neuropsychiatric Service, Cushing Veterans Administration Hospital, Farmingham, Mass.

The transcribed interviews also showed that the residents tended to pay attention for the most part to only manifest content of the patient's speech and behavior and frequently guided the patient's associations in the direction of their own personal interests and problems. There were definite inclinations to become lost in historical material and to misunderstand or be unaware of the transference and counter-transference relationships as well as the reality situation.

We had realized that good psychotherapists could not be made over night but felt that psychotherapy could be taught in a more definitive manner. As the basis of insight therapy lies in a recognition of the unconscious we decided to lay more stress on the reality value of the unconscious and tried to teach the residents how to use the Associative Anamnesis technique developed by Felix Deutsch.[2,3] We felt that once the doctor had developed the faculty of "listening with the third ear" he would understand what he was doing and why. We also considered that a better understanding of the unconscious and its manifestations would result in less need or at least a better utilization of therapeutic adjuncts such as hypnosis and narcosis and give the therapist more freedom from the anxieties resulting from therapeutic disappointments and excessive expectations.

The Associative Anamnesis is the name given to a method of history taking which has been adequately described by Deutsch.[2] It forms the basis of what he calls "Sector Psychotherapy."[4] Correct application is in the literature.[4] Sector Psychotherapy is based on the dynamic genetic concepts of psychoanalysis with two principal modifications of them: first, the material as procured through the Associative Anamnesis is utilized in the place of that procured in psychoanalysis by free association; second, the limited goal in the therapy is the alleviation of only a certain incapacitating conflict and not those of the entire personality. There are other applications of psychoanalytic concepts. At the beginning of treatment, a positive identification is important to obtain material. Identification of the patient with the therapist is facilitated by incorporating the most often repeated words or expressions of the patient into the speech of the therapist. This identification is continually strengthened by the maintenance of the continuity of associations and their intensification through repetition. By a continual linking of behavior patterns in the past with similar ones in the present reality situation the patient's behavior patterns become clarified and deeper material becomes accessible. Use of the patient's own words by the therapist aids in (1) the development of an early identification with the therapist, (2) provides the link which makes conscious the unconscious motivations of the symptom, and (3) produces a positive reaction on the part of the patient to the therapist. This aids also in the splitting of the patient's ego, as in psychoanalysis, into an adult, intellectual, "observant" portion which can ally itself with the therapist and thus achieve better control over a more infantile, emotional and "experiencing" portion. The division of the ego into these two parts permits the patient to observe the discrepancies and the irrationalities of his behavior in the present as compared with his behavior in the past. This insight in conjunction with the support of the therapist enables the ego of the patient to alter its defensive attitude and tolerae as well as conrol anxiety-provoking unconscious material when it is brought to the surface or evoked by the reality situation. Development of rapport with the therapist also has another important effect. Through the introduction and incorporation of the therapist's own words and phrases, the patient's words become modified, leading to a dissolution of previously unconscious association chains which are tied together through ideational and sensual content, and facilitates their replacement by new and more reality-tested chains of association. The entire process has been thoroughly described by Deutsch in his new book.[4]

It is recognized both theoretically and practically that a sector of a person's life or a certain conflict cannot be analyzed without producing or necessitating changes in the entire personality. For this reason, our goals in this hospital setting remain limited to the abolition of certain presenting symptoms and the restoration of the patient to a socially useful level of existence. At times

our goal has been simply amelioration of the patient's symptoms to the extent where he can receive out-patient department treatmen at a Mental Hygiene Clinic. In most cases, the identification with the doctor and the interpretation through clarification and confrontation leads to a making conscious of unconscious material and a strengthening of the patient's ego to such an extent that he is able to settle a great deal of conflictual material by himself after his discharge from the hospital.

In addition to its value as a type of therapy, the Associative Anamnesis Sector Psychotherapy technique has been especially useful for teaching purposes. It promotes a more rapid development of a faculty in reading between the lines or, as it has been called, "following the red thread of the unconscious" in the manifest productions of the patient. The acquisition of this facility, it is felt by us, is a basic necessity before understanding other forms of insight therapy in order that the doctor have some idea of what he is doing and why he is doing it. Psychotherapy is prevented from becoming wild psychoanalysis and bogging down in a morass of speculative interpretations, exhortations and seductions. This technique enables both the resident and the supervising psychiatrist to develop not only a better understanding of what is happening but an increased ability to explain psychodynamics on the basis of the individual case material rather than on didactic and authoritative clinical experience with similar cases, both of which we have found the resident tends to meet with resistance. It promotes not only a proper evaluation of the unconscious material but also a better understanding of the transference situation. This is especially important in view of the growing familiarity of residents in psychiatry with psychoanalytic literature and the inevitability of the appearance of disguised resistance and rejections. Residents also are better able to avoid excessive expectations from their therapeutic endeavors and get a better realization of what the patient's problems are and the role they play in therapy.

Since a teacher-student relationship is no less delicate than a patient-therapist relationship, we use a graduated approach in training. The first month on the Open Ward Service is devoted to recording only the resident's initial interviews with patients and at the resident's request. These recordings are transcribed by the secretary and discussed in conferences on therapy attended by the residents and senior staff and held three times a week. During the conferences, the group is encouraged to discuss these interviews in a constructive and friendly manner, and the Associative Anamnesis technique is taken up and critically examined both theoretically and in connection with difficulties encountered by the residents in their own sessions. After four to six weeks, the patient-doctor sessions are sampled unknown to the doctor and discussed in the same manner. During these discussions, problems relative to character traits of the residents frequently appear and are handled as tactfully as possible. We anticipated resistance to this technique when it was first set up but this has not occurred.

During the first half of the six-month training period, the patient-doctor interviews are transcribed and discussed. The details of the individual resident's technique are carefully evaluated by the group, the senior acting as a moderator. When it has become apparent that the residents have acquired some facility in applying the principles of the technique, the interviews are played back in toto from a wire or tape recorder and criticized as a whole. Some of the later conferences are devoted to special problems of technique, such as the handling of the various types of the psychoneuroses and psychosomatic diseases, and such common resistances on the part of the patient as acting out, isolation of material, intellectualization, verbosity, undue reticence in speaking, and hyper-emotionality. We also found that a selected group of papers[5-12 incl.] related to the fundamentals of therapy were of great value in clarifying the resident's ideas concerning the use of this technique.

There comes a time when the resident, in spite of his personal limitations, becomes sensitized to and aware of the unconscious verbal productions of his patients and the repetitive nature of his own difficulties as well as the patient's. Consequently he develops an understanding of the meaning of

the transference. It is then that the most difficult step of all must be taken, i.e., the coordination of this technique in order to produce therapeutic results. This can be done not only by learning to understand the unconscious meanings of the patient's verbalizations and the ego defenses, but by a continual evaluation of the reality situation which includes the secondary gain resulting from pension, hospitalization, and the avoidance of adult responsibilities, as well as other obvious situational difficulties. If the associative anamnesis-sector psychotherapy type of approach is utilized well, all of these factors can be handled and integrated into a reasonably successful type of insight psychotherapy.

In order to illustrate this type of interviewing, an unretouched fragment of a resident's initial interview with a patient is presented.

Case Report

The patient was a 53-year old veteran who was admitted to the Surgical Service complaining of low back pain, pains in the neck, nausea and vomiting, nervousness and depression of indefinite onset. The medical workup was negative. His back pains had been with him since he was 27 years old and came on after lifting a tub full of clothes from a stove. At that time, he had felt something give way in his back and from then on had periodic episodes of pain which made it difficult to work. At 48, a coccygectomy was performed, and at 50 a hemorrhoidectomy. Sixteen months ago he had been operated on for a ruptured intervertebral disc in the lumbar area. Since this latter operation, his back pains had become worse, and he had to wear a support which helped the pain in his back but made his legs feel numb and weak and led to feelings of nervousness, as well as nausea and vomiting. He had been to numerous physicians on the outside as well as chiropractors and osteopaths and had tried all types of manipulations, physiotherapy, vitamins, nerve tonics, etc., but had been unable to find relief. He felt that he needed another operation and at times became depressed and felt he would be better off dead. The past history revealed that he was the fourth of eight children. According to the patient, when he was quite young, his father beat him frequently and on numerous occasions told him he wished he had been a girl. Patient himself wished many times that he had been one so that he could have worn a corset all his life and received support for what he believed was a congenitally weak back. When he was 17, his mother, who had always protected him from his cruel father, died, cause unknown. He had guilt feelings about this, the nature of which were, according to him, that he could have helped her more and made her lot easier. After her death, he served a six-year hitch in the Army where he made a moderately good adjustment. Following this he married, had three children, and was then deserted by his wife for another man because, he felt, of his poor sexual abilities. He remarried and four years ago his second wife left him for the same reason as did the first. With his second wife, he had been more often than not completely impotent. For the past four years he had been living by himself, his children by his first wife living with his second wife's relatives. Two years ago his father died of heart trouble. During the interviews, he showed alternately periods of apathy and agitation, fearing that he was going through the change of life which meant to him a great deal of suffering. He gave detailed descriptions of how much he was suffering and appeared to derive some satisfaction from his ability to endure it. Most of his interviews revolved about his feelings of inadequacy, impotency, and inability to play a masculine role. His attitude towards doctors and others appeared to be a passive receptive one, and he frequently expressed feelings of utter helplessness as well as reactive feelings of rebellion and rage against his lot. Later in his interviews he verbalized strong needs for a maternal, protective figure and much hostility because his needs were not gratified. This attitude was tied up with his experiences with mother and father alike, both of whom he felt had exploited him and prevented him from expressing his masculinity. His symptoms gradually lessened and after three months therapy he was discharged from the hospital at his own request and returned to work.

Doctor Interviewing the Patient

D. Would you like to tell me what problems bring you to the hospital?

False assumption that patient knows he has an emotional problem. Doctor should have only asked: "Why do you come to the hospital?"

P. Well, there's something bothering me; it could be *nerves;* I don't know.

D. What do you mean by *nerves?*

. . Using patient's own words.

P. Well, I get terribly *nervous.* I don't know, I imagine it's because I have this *numbness,* you know.

D. *Numbness?*

P. Yes.

D. How's that?

P. When I wear the *support,* it makes me *nervous.* I imagine it's the *numbness* that makes me that way.

Patient unknowingly links nerves-numbness-support.

D. What do you mean by numbness?

P. Well, it's a *dead feeling* like, you know *(further linking of key words by patient),* and *you lay in bed* and *your legs are numb,* and you keep them *moving* all the time to try and get the circulation, like a, you see, I usually *rub* my toes when I *lay in bed* and that helps a little, I was taking some treatments before I was *operated* on. Dr. H. said that I shouldn't wear the *support (Dr. H. denied patient*

the support patient felt he needed), he said that stops the circulation; *I got to have support* even so.

D. The *numbness* gave you a *dead feeling?*

Dr. continues to link key words together.

P. Well, it's a *numbness,* you see, and I, I have *to keep my legs going* all the time. That's the way it feels to me. It's *been worse since I was operated on.* It wasn't quite so bad before I was operated on. I had some *numbness* before I was *operated* on but it seems *after the operation it was worse.*

D. You were operated on?

P. Yeh, *my back.*

D. Your back?

P. Yes, a disc.

D. You had a *disc in your back?*

P. I had it up—the disc they operated on and they straightened it, I guess, or something; they took an x-ray, and it was like that, bent, you know. It's a *strain I got years ago.* That's the way it showed it in the x-ray, *before I was* operated on, and the *doctor* went and *operated* on me.

Patient expands, shifts to other area in body—"operation" is the link. Expanding ideas—with repeated use of same key initial words. A lead into the past.

D. You say it was *bent?*

P. Yeh, it was *bent,* that's the way it looked to me, *my spine,* I suppose that is what they call a *disc,* I don't know. Well, anyway, they told me it was a *disc* they operated on, Dr. M. I don't know nothing about the spine or anything else about it, you know, but that's what they hold me.

D. Yes, of course. *So this disc is bent?*

P. Yeh, and they *straightened* it, see?

D. They straightened it? What do you mean?

P. Straightened it. I suppose it's *the spine,* the *disc.* What is a disc, I don't know myself. How would I know. They x-rayed it after I was *operated* on and they x-rayed it here and it looked all right to them. Dr. S. told me so. Of course, I didn't have so much trouble *before I was operated on. (Another lead into the past.)* It seems now something has gone *wrong.* It's *perfectly numb.*

D. As you understand it, this *disc* was sort of *bent down?*

P. Well, it was *bent.* I don't know whether it was bent down, or sideways, or, but that's the way it looked to me. I saw the x-rays.

D. You saw them?

P. Yes, and it looked like that, and I suppose *they straightened it* out. Of course, I know my back feels better, you know. I mean, you know, I don't have those *pains around my shoulders* or my *arm don't bother me,* or if I should *happen to walk along* and *kick* anything it *wouldn't bother me that way. ..It used to.*

New associative chains with repetition of key words.

D. When you *bent your finger like that* to show that the *disc is,* well rather what the disc was, and then how do you think they, how did they *straighten* it, as you say?

Dr. uses patient's behavior or mannerism as well as words in developing the associations.

P. I don't know. I haven't seen it naturally. Just what Dr. S. told me, the x-ray looked good to him. I saw it before I was *operated on.*

D. You saw it before you were *operated* on?

P. Before I was operated on.

D. And that's what you, as you show me with your finger?

P. Yes.

D. You say it was *caused by a strain?*

Dr. making and testing associative connections, still using only patient's words.

P. Yeh, *lifting, years ago.*

Entry into the past.

D. What sort of a strain?

P. *Lifting.*

D. Lifting?

P. Heavy lifting. I felt it when I was lifting. I felt something go. Oh, this was years ago, in 1922 or '23, and when I let go I felt this thing go, you see, whatever it was and of course I *didn't bother with it* any more, you know, and it kept *getting worse* all the time and if I had only knew at that time, you know, I'd go somewheres, some doctor, and he could probably fix me right away, *but like everything else I passed it off.*

Dr. missed very important cue to past and a characteristic pattern.

D. So as you lifted, you say, you felt something go?

P. Yes, I *felt it in my back,* when *I* let go, I *remember* that just as clear.

D. You can still *remember* that feeling?

P. No, I mean when that happened.

D. You *remember that far?*

Keeping patient in the past by using "remember."

P. Yes, 1923, I guess it was, *maybe 1922.* You know, *working around the milk trucks ("milk trucks" is a link to the past),* that didn't help it any, see, I used to peddle milk for a company, you know over in Sherbourne. Well, I went to work for them when I came down from Vermont. I used to peddle *milk* and also pasteurize *("milk" probably over-determined),* and I had about 300 quarts to deliver, you know. Sometimes *I had somebody to help me, you know (needed "somebody" to help [support]),* and I found out by *jumping off the truck* and *jumping on,* you know, it made me worse, see, and I also got those *pains in the back of my neck,* you know *(punished for the jumping by pain in the back of his neck);* the *pain got so terrible I had to give it up,* so I just worked around in the *milk* room, you know. *I stayed off the truck* and I found out by staying off that truck and *not throwing so much stuff* around, you know *(lifting "milk" cans dangerous),* that it wasn't quite so painful, you know, and now I don't know if it's the dampness that's *doing this* to me now in the *milk room* or not. *("Milk" room "does it to him".) I don't know, I'm sure.* I don't think so though because the floor is round like and the *water* never stays on the floor *(turns from "milk' 'to "water"),* just rolls right off all the time, never stays on the floor. I wear rubbers any way.

D. You *remember* this *feeling* of something letting go in your *back?*

Keeping after key words.

P. Yeh, like *a little snap like,* you know. I could even *hear it,* you know, when it went in my *back* at that time.

D. Snap—what do you mean?

P. Well it was just a little noise I made when *I let go* of this *boiler* I had full of clothes, taking it from the stove. *(Dangerous "water" boiler.)* I lifted it up that way, pulling it off from the stove, and put it down on the floor, and just as *I let go* I had this *snap, it let go in my back,* see, and I've had *trouble* with it ever since. Of course it's been getting worse every day now and that was a pretty heavy *boiler* of clothes, you know, *full of* water.

D. You were at work, you were *lifting?*

P. I was at *home.*

D. You were at home?

Patient introduces home for the first time without Dr. asking direct questions.

P. Yeh.

D. Lifting a boiler and you felt a snap?

Dr. missed cue re home life and the meaning of "home" which would have given him the opportunity of linking up "old" and "new" home, i.e., the past and the present and to learn about the meaning of "milk room."

P. Yes, as I put it on the floor, after I lifted it on the floor I felt it go.

D. You were lifting a boiler with the clothes?

P. Full of clothes.

D. You were washing?

A direct question admissible because of the previous verbal content of the patient.

P. No, I wasn't washing, my *wife* was.

First person in home introduced. It is the new home where a woman appears.

D. Your wife?

Who was in the old home?

P. Yeh.

D. I *didn't know* you *were married.*

The interviewer makes the mistake to reveal that he himself is an "I don't know" kind of person. The phrase should have been again: "Your wife?"

P. I was *then,* yeh. (Long pause.) *(Another lead into the past. The pause indicates that "wife" is a relevant figure. Pt. asked the ambiguous question, whether that "what he was talking" had something to do with his "nervousness.")* Don't you think this has a lot to do with it, this what I was talking. Making me *nervous* that way, don't you imagine that has something to do with it. Making me feel this way, don't you imagine that has something to do with it. Making me feel this way, like I was last night. I'm right next to the door there and they're going in and out all the time and it goes on up to one or two o'clock. *("People" going in and out cause nervousness.)* Before that I was just laying there, that's all.

D. This *support,* you think, has a lot to do with your nerves, you say.

Interviewer missed linking of the present with the past.

P. Yeh, sure. If I didn't wear it, I get terribly *weak* from my hips down.

D. Get weak?

P. If I don't wear the *support.*

D. What do you mean, you get weak?

P. Well, I don't feel like *working,* walking or standing or anything, I just want to *sit down* again, you see, when I don't wear the *support.* If I could get along without it, I wouldn't wear it five minutes. Just what the doctor said to me, try to get along without it. Wear it one day and leave it off the next. Well, I've done that but I couldn't, I had to wear it.

D. This weakness, what do you mean by *weakness?*

Doctor continues to "follow the thread" by expanding meaning of "weakness."

P. My legs get *weak* from the hips down if I don't wear the *support.* I get so *weak* that I want to sit down somewheres. It seems like that I NEED SOMEONE TO HOLD ME if I don't wear the *support. (Support becomes personified. Who is "someone." Is it his wife? Who was it in the past?)* It's one or the other. I get those *pains* in the *back* of my *neck* too.

D. So if you don't have the support, you say you get *weak.*

P. Yes.

Patient himself links "nerves-weak and support by someone" together.

D. And nervous?

P. Well, I'm not quite so nervous when I haven't it on.

He has a need to be supported by someone and is "nervous" without the "supporter."

D. When you hanven't got it on?

P. When I haven't got it on, I'm not quite so *nervous,* but it seemed to me that when I feel *weak,* you got to wear it *tight* to have any *good* and when I wear it *tight* like that I get *terribly nervous. (But he is also "nervous" with the "supporter.")* I don't know. I seem to be *run down* all the time too. I don't know whether that has anything to do with it or not. It sure isn't because I *don't live a good life. (He connects weakness and nervousness with being good or bad. An important new lead into the past. Doctor should have asked, "You have not led a good life?")* I don't like to have to wear a *support,* but if I have to I have to. Don't you think I look rather *thin? ("Thin" means good.)*

D. You think you are very thin?

Doctor does not get trapped into answering question but continues to elaborate the material.

P. I know I am, I feel it.

D. You feel *thin?*

P. Sure, feel it right in my *face.*

D. How can you feel thin?

P. Well, the way you feel, that's all. I can tell by the *way my eyes act* too sometimes, you know. Guess I NEVER *was very fat* anyway. *("Fat is bad, but he wishes also not to be too thin.)* But I shouldn't be as thin as I am, I don't think.

D. You never were fat?

Another lead into the past! and seen by the resident.

The development of the theme "nervousness" led to the elaboration of the patient's conflict over "needing support" and demonstrated how he somaticized his conflict. Not having support expressed his feelings of weakness and helplessness and the need to have someone hold him up. However, being supported resulted in pain and nervousness as an expression of anxiety over being supported. Expressed technically, this fragment of an interview revealed ambivalence towards a supporting object and his conflict over his passive dependent needs. The ambivalence conflict was expressed through the words "you know" or "I don't know" which the patient used thirty-two times in this short interview. The above portion of the interview lasted for approximately fifteen minutes. The next thirty minutes was taken up by the patient in describing how he had had his "tail bone" cut off by a doctor to relieve his feeling of pain and discomfort. He was then led into the past and verbalized his feelings concerning both mother and father. He thought about mother and compared her with the poor cow whose picture he had seen in "Life" Magazine, frozen to death, standing on her feet, up and about to the very end, how she protected him from father ,and how guilty he felt because he had not made her lot easy. He then talked about how cruel father had been to him and how father had repeatedly beaten him across the back and the legs. Mother had frequently saved him from whippings by his father, and he remembered his father coming home after mother's funeral and saying to him, "Well, she is out of your way now." He wondered why father had said this because she was such a wonderful mother even if he did not realize it until after her death. He wondered whether or not if he had worked for mother more he could have prevented her from dying so soon. His conflict over his passive dependent needs and ambivalent attitude towards both father and mother could be superficially but directly linked up both in the past and in the present.

Summary and Conclusion

Teaching the principles and procedures of Insight Psychotherapy is difficult. In it is implied the development of the therapist's ability to become aware of the unconscious motivations of a symptom, the emotional basis of the patient's relationship to the therapist, the repetition of infantile patterns in present day behavior, and the utilization of the therapist's knowledge to induce the patient to modify his present thought patterns and behavior. A method is presented using recorded interviews and the Associative Anamnesis Sector Therapy technique as an approach to the solution of this problem. A fragment of an interview and its discussion has also been presented.

REFERENCES

1. Murphy, W. F., and Weinreb, J.: "Problems in Teaching Short Term Psychotherapy." *Dis. of Nerv. Syst.,* IX, No. 4, April 1948.
2. Deutsch, F.: "The Associative Anamnesis." *Psychoanal. Quart.* VIII, 354-381, 1939.
3. Deutsch, F.: "Psychological Methods of Obtaining Medical Information." *Acta Medica Orientalia,* V, No. 8, August 1946.
4. Deutsch, F.: "Applied Psychoanalysis—Selected Objectives of Psychotherapy." *Greene and Stratton, Inc.*
5. Deutsch, F.: "The Production of Somatic Disease by Emotional Disturbances." *Res. Publ. Ass. Nerv. and Ment. Dis.,* XIX, 271-292, 1937.
6. Deutsch, F.: "The Choice of Organ in Organ Neurosis." *Int. J. of Psychoanalysis,* XX, Parts 3 and 4, 1939.
7. Deutsch, F.: "The Psychosomatic Concept." *Acta Medica Orientalia,* VII, No. 3, March 1948.
8. Deutsch, F.: "The Use of the Psychosomatic Concept in Medicine." *Bul. Johns Hopkins Hospital,* LXXX, No. 1, 71-85, January 1947.
9. Deutsch, F., and Nadell, R.: "Psychosomatic Aspects of Dermatology with Special Consideration of Allergic Phenomena." *The Nervous Child,* V, No. 4, October 1946.
10. Deutsch, F.: "Prophylactic Aspects of the Malnutrition Problem." *The Nervous Child,* III, No. 3, April 1943-44.
11. Waller, J. V., Kaufman, M. R., and Deutsch F.: "Anorexia Nervosa—A Psychosomatic Entity." *Psychosomatic Medicine,* II, No. 1, January 1940.
12. Finesinger, J.: "Psychiatric Interviewing." *Am. J. of Psychiat.,* CV, No. 3, September 1948.

Authors' Note: This paper is sponsored by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Evalvation of Results from Leukotomy in Schizophrenia

MYRON FELD, M.D.

Tomah, Wisconsin

In selecting leukotomy as a therapeutic measure the psychiatrist tends to be properly conservative. This is especially true in the medical service of the Veterans Administration. In every instance leukotomy is proposed only after the patient has had adequate therapy of a less drastic nature. In the schizophrenic reaction types the duration of the psychosis is one of the major considerations; in short, the patient must have reached a stage of chronicity lasting at least eight or ten years and, in the instance of schizophrenia, all other modern therapies were employed adequately and without substantial or lasting improvement. This would comprise 30-40 insulin comas; 20-40 electric shocks, and psychotherapy to a degree that rapport would permit. In addition to these considerations the staff attitude in some instances includes serious consideration of the persistent manifestations of the psychosis, thus taking into account what might be termed psychic pain in the form of fear and terror or attitudes that appear to be the result of great mental distress, as well as assaultive behavior. An effort is therefore made to weigh the probability of leukotomy serving to relieve the patient or alleviate such distress. With that as the therapeutic objective and the added possibility of bringing about such changes in the psychotic reaction as to lead to more satisfactory adjustments outside of a controlled environment such as a hospital, the problem of selection is entirely a psychiatric decision. Any procedure that may help even slightly in arriving at a decision in accordance with the specifications mentioned should be welcomed.

As pointed out by Kalinowsky and Scarf[1] statistical reports are of little help. Every case should be weighed in its own particular setting. A review of the published results from leukotomy in schizophrenia shows a wide range of so-called recovery or substantial improvement. Greenblat, et al[2] reported on the particular symptoms or manifestations that were relieved in 147 cases. They summarized their results in terms of 65% relieved from tenseness, fear, worry, and alleviation in hallucinations, delusions, etc. Reitman[3] reported 24% in 250 cases in which the improvement was sufficient to permit discharge from the hospital. Others have reported as low as 10% in schizophrenia, while some have claimed favorable results in as high as 70%. It is quite obvious that the measurement of improvement, or what has been termed good social adjustment, is by no means standardized.

In dealing with schizophrenic reaction types psychiatrists must attempt to answer the question—can this or that distressful symptom be affected favorably, or what manifestations are likely to persist unaltered. In practically every case the near relatives are deeply concerned since permission for the operation is required. To quote statistics, ranging from 10% substantial improvement to 60 or 70% degree of improvement is not conveying much information upon which a layman may make such a radical decision. Therefore it is believed that any procedure which might contribute a measure of information on the possible outcome is helpful. With that in mind, 10 cases of schizophrenia in whom leukotomy was elected were given deep narcosis by means of a barbiturate as a preoperative examination.

The procedure is as follows:

1. A complete psychiatric interview, so far as such is possible at the conscious level; rapid induction of deep narcosis with Sodium Amytal by intravenous administration.

2. Observing and noting the behavior and responses of the patient after being aroused from a brief period of unconsciousness that reaches practically the level of surgical anesthesia. This postnarcotic stage usually

permits interrogation for a period of 1½ to 2 hours.

3. The method of amytalization employed conforms to that first suggested by Bleckwenn[4] and subsequently carried on by other members of the Wisconsin group.[5]

Briefly stated, the following technique is employed: Patient has had no food or fluid at least for a two hour period before the intravenous injection. One gram of sodium amytal is dissolved in 20 cc. of freshly distilled water. As a precautionary measure picrotoxin is made available. The intravenous injection of the Sodium Amytal solution is given at the rate of 1 cc. per minute and continued without interruption until corneal anesthesia is produced. Usually 10—12 cc. will be required in the average individual weighing 150 pounds. In some instances the entire 20 cc. will be required to induce a sustained stage of unconsciousness. The administration of the drug is stopped when the corneal reflex is absent. Within a few minutes attempts are made to arouse the patient by placing cold wet cloths over the face, on the chest, and also by voice. These efforts should be persisted in even when wakefulness and responsiveness are delayed. While considerable time can be saved by using picrotoxin, the objection to this more rapid return to consciousness is that it may shorten the period of interview—what the psychiatrist needs in order to make the most use of deep narcosis. It is necessary for the examiner to persist with questions until the patient becomes more or less spontaneous in his talk. After a satisfactory period of observation and interrogation the patient can be permitted to relax but there should be continued attendance by a nurse or qualified aid during the period of sleep that always terminates this procedure. The depth of the post-narcotic period can be determined by subsequent memory or lack of memory concerning questions, answers, and other happenings during that period.

The critical post-surgical evaluation is made after two or three weeks as a minimum and the observations and manifestations of the patient compared with those observed during the post-narcotic period.

In 9 of the 10 cases in which this schedule was completed, it was found that the post-operative results resembled very strikingly the conditions observed during the post-narcotic stage.

The leukotomy in the cases studied was performed by Dr. Henry Suckle, neurosurgeon consultant to the hospital.

Two typical cases will serve to illustrate the similarity of the postsurgical results with those transient manifestations observed during the post-narcotic stage but not in its entirety since all of the environmental factors to which the patient is reacting are not the same; nevertheless, in the fields of major interests, emotional attitudes, false ideas and false sensory perceptions which generally go to make up behavior reactions at the conscious level are for the most part the same.

The first case is that of Z.H.K., World War II veteran who was born March 31, 1912, and who has been known to many veterans' mental hospitals to be an alcoholic and mental defective. The first hospitalization occurred in 1943 at Downey, Illinois. At that time he was very manneristic and out of contact, however having lucid intervals and was able at these times to work around the ward. He had auditory and visual hallucinations and was given a diagnosis of hebephrenic schizophrenia. In 1947 he was transferred from that installation to the VA Hospital, Tomah, Wisconsin. While in this hospital he has been out of contact and unable to do any ward work for the past two years; and only occasionally would he so much as say "good morning" to any of the personnel. He often had to be given hydro-sedation because of overactivity and was very manneristic, bowing down and using his thumb and forefinger in a clicking manner. It was noted that he was responding to auditory and visual hallucinations. Prior to amytalization no contact or answers could be had from the patient. The veteran was placed under 12 grains of amytal and was taken down to absence of corneal reflex and revived by the use of cold towels. Under the effects of the narcosis he admitted some hallucinations but did not respond to them. However, when his pre-narcotic manner-

isms were mimicked he was able to explain them, stating that he was feeling mink and later that he was using a teletype. The mink was equivocated in his mind by women. After about 30 minutes of questioning he began to make suggestive remarks to the nurses. Ward personnel present at the interview were surprised to find that the patient was well oriented as to time, place and person and that he could name the ward boy and the nurses, and also could recognize the psychiatrist. He could give information concerning his family, some of the places he had worked and his Army experiences but could not work even the simplest mathematical problems. This last might be expected in view of his very low I.Q. to begin with. When asked what he would like to do when he got better, he said he would like to go out and own a mink farm and have a pond and raise bullfrogs for selling. He became very talkative and active but not assaultive. Affect became improved almost to the point of appropriateness. His memory was definitely improved since he was out of contact before and his mood was rather jovial though judgment still remained poor. He realized where he was and thought that he needed help; he did not quite understand how he had gotten in the hospital or why. For two days following the amytalization the patient was hyperactive and had to be given continuous tubs. Forty-eight hours after his hyperactivity a bilateral prefrontal lobotomy was done and periods of interviews covered up to three months postoperatively.

The patient has remained rather restless; however, he now participates in ward activity with the Gray Ladies. He is oriented; his memory is vastly improved. He is making some plans for the future, but not that of maintaining a mink farm. He wants to go back to work in a shoe factory where he once worked. The patient still has some auditory hallucinations but does not react to them. If stimulated, he will repeat his manneristic performances, duplicate them and explain them as sending messages; however, he will not do this voluntarily. He reads the newspapers on the ward and his behavior is excellent although his intellect is still functioning at a low level. The relatives who have visited him are astounded at the improvement he has shown.

Although this patient may not be sufficiently improved so as to be able to leave the hospital and take his place in society, he will be able to function on an open ward, perhaps, and do work around the hospital. He will not require any great amount of nursing or attendant care. His condition under amytal was approximately the same as that we see now postlobotomy.

The second case is that of H.R., 38 year old white veteran of World War II. During his service career he spent two months in a naval hospital and then was given an N.P. discharge in 1942. On November 7, 1947 he was committed to the Mendota State Hospital, which was then a veterans' mental installation. At that time he had active auditory hallucinations, delusions of being poisoned and thought that spies were after him. The patient was given a diagnosis of paranoid schizophrenia. Personal history reveals that in his home town he was known as a recluse and a night prowler for many years prior to his hospitalization. From his wife it was learned that he was very active sexually, having intercourse eight times a day at home and frequent extramarital relations whenever possible. On December 3, 1947 he was transferred to the VA Hospital at Tomah, Wisconsin, at which time he was preoccupied with sexual thoughts. At times he was disoriented and often attacked the nurses who feared him and referred to him as looking like "a wild animal" when after them. He had failed to respond to any of the therapies. Just prior to amytalization the veteran was interviewed; he was well oriented at the time but showed no insight. He made degrading remarks at the nurse who was present in the room. He was able to work simple mathematical problems. He denied any hallucinations and said he did not know why he went after women, probably because they beckoned to him. He was then placed under 12½ grains of sodium amytal and reawakened.

At this time he admitted to auditory hallucinations. He stated, "God tells me to go after women and bring them to, that's what

they are meant for." He also complained of a buzzing noise in his ears which caused him to curse. The patient was well oriented for time, place and person but memory remained poor. He showed, in general, poor judgment by trying to grab the nurse while two attendants were holding him. He showed no degree of insight whatsoever; he was able to answer simple mathematical problems, but his abstract thinking was impaired. He did not think that he needed to be in the hospital, nor did he want any help from the physicians. The examiner was hard put to get him to discuss anything but women. The veteran underwent a bilateral prefrontal lobotomy 48 hours later.

Following the lobotomy, for three weeks he did not bother any of the nurses on the ward; nor did he cause any particular trouble. However, the attendants were on continual watch and at the end of this time he tried to attack one of the nurses and relapsed into almost the same condition as preoperatively. He has shown no improvement whatsoever and has to be watched closely.

I believe this case represents one in which, if we had had some means of prognosticating beforehand, the lobotomy should not have been done. Under amytalization he showed only slight, if any, improvement and then following lobotomy the same condition was found. In addition, we might add that there was no change in affect under the amytal except for a giddiness caused by the drug.

As already mentioned, the psychiatrist is confronted with the difficult problem of explaining to the patient's relatives what can be expected or hoped for from leukotomy. It is believed, on the basis of this experience, that the testing under deep narcosis reveals fairly reliable data, especially concerning the predominating symptoms and manifestations of the psychosis insofar as these can be substantially altered in the nature of relief by surgery. False hopes and subsequent disappointment can be guarded against. It is believed this alone fully justifies an attempt to get more information before the psychiatrist advocates leukotomy in a specific case and the relatives are called upon to give their consent.

It is fully realized that the number of cases studied is entirely too small to justify any generalization; therefore this report is offered as a preliminary finding with the suggestion that others should include deep narcosis as a preliminary method of examination prior to leukotomy.

REFERENCES

1. Kalinowsky, L. B. & Scarff, J. E.: *Am. J. of Psychiat.* 105: 81-35, August, 1948.
2. Greenblat, M., Arnot, R. E., Poppen, L. L., Chapman, W. P.: *Am. J. of Psychiat.* 104: 361-368, Dec., 1947.
3. Reitman, F.: *Am. J. of Psychiat.* 105: 86-89, Aug., 1948.
4. Bleckwenn, W. J.: *Wis. Med. J.*, Dec., 1930.
   Bleckwenn, W. J.: *Arch. of Neurol. & Psychiat.* 24: 365-372, August, 1930.
5. Loevenhart, A. S., Lorenz, W. F., Martin, H. G., Malone, J. Y.: Stimulation of Respiration by Sodium Cyanide and Its Clinical Application. *Arch. Int. Med.*, 1918-21: 109-129 (March).
   Loevenhart, A. S., Lorenz, W. F., Waters, R. M.: Cerebral Stimulation. *J.A.M.A.* 92: 880-883, Mar. 1929.
   Lorenz, W. F.: Some Observations on Catatonia. *Psychiat. Quart.* 4: 95-102, June, 1930.
   Lorenz, W. F.: Criminal Confessions Under Narcosis, *Wis. Med. J.* 246-250, Apr., 1932.
   Reese, H. H.: A Method of Counteract Intoxicating Effects o fBarbituric Acid Drugs. *Wis. Med. J.* 530-532, Aug., 1933.
   Lorenz, W. F., Reese, H. H., Washburns, A. C.: Physiological Observations During Intravenous Sodium Amytal Medication. *Am. J. Psychiat.* 13: 1205-1213; May, 1934.
   Bleckwenn, W. J., Hodgson, E. R., Herwick, R. P.: A Clinical Comparison of Picrotoxin, Metrasol, etc. *J. of Pharm. & Exp. Ther.* 68: 81-88, May, 1940.
   Bleckwenn, W. J., Masten, M. G.: Antidotal Treatment of Barbiturate Intoxication. *J.A.M.A.* 111: 504-507, Aug., 1938.

The foregoing article has been reviewed in the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions contained herein are the result of the author's study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Non-Convulsive Electro-Stimulation In Insulin Coma

(A Preliminary Report)

FRANCIS H. HOFFMAN, M. D.
CHARLES A. WUNSCH, M.D.
Traverse City, Michigan

This report is concerned with some preliminary observations which indicate that the electrical convulsive threshold is lower during insulin coma than during sodium pentothal anesthesia and that non-convulsive electrical stimulation aimed at the diencephalon with electrodes positioned bilaterally above the ears tends to decrease the depth or waken patients in insulin coma. Some degree of elevation of the blood sugar levels was also noted.

A pulsating direct current, by design a relatively inefficient convulsive agent, was used in the manner initiated by Hirschfeld for non-convulsive electrical stimuation of patients anesthetized with sodium pentothal. The technique as employed by Hirschfeld involves the intravenous injection of sodium pentothal to and beyond the point of loss of the lid reflex. Hirschfeld then applies electrodes bilaterally just above the ears and stimulates with a current of 10 ma. for 20 seconds. The stimulation is then reduced to an amperage permitting respiration to be resumed, usually below 5 ma., and this stimulation is continued for two to five minutes or to such point as it is no longer covered by the pentothal anesthesia. In association with Dr. Paul H. Wilcox we confirmed the observations of Hirschfeld and others that this electrical stimulation tended to awaken patients from the sodium pentothal anesthesia.

The present investigation was undertaken to determine whether or not a similar stimulation would awaken patients from deep insulin coma. The patients stimulated were those who were at the time receiving coma doses of insulin on the insulin service at the Traverse City State Hospital. The length of coma at the time of stimulation ranged from twenty minutes to two hours. The usual criteria for the onset of coma were observed with the final criteria being absence of response to vigorous shaking and to painful pinching of the ventral surface of the upper arm. The electrodes were applied as in the Hirschfeld technique. Stimulation was initiated with a current of 0.5 ma. and was then raised rapidly to the highest level permitting regular respiration. Usually this level was between 3 and 4 ma. The stimulation was continued for a total time of five minutes.

In two patients an attempt was made to duplicate the Hirschfeld technique, using 10 ma. initially, but in both of these patients a grand mal occurred within three to five seconds following the beginning of stimulation, demonstrating the lowered convulsive threshold in patients in insulin coma as compared with patients under sodium pentothal anesthesia. Specifically, with this type of current, no patient anesthetized with sodium pentothal in our series (300 treatments) or in Dr. Hirschfeld's series had a convulsion with a current of 10 ma. given for a stimulation time of 20 seconds.

Stimulation, conducted on the basis of clinical observation only, quickly demonstrated that this stimulation did tend to decrease the depth of insulin coma or even awaken the patients so that they could take their glucose orally. The patients who awakened regained consciousness five to ten minutes after the termination of stimulation.

Because of these encouraging clinical observations blood sugar levels were run on the patients thus stimulated. The following chart is a summary of our findings. In this chart the column headed "Duration of Coma" indicates the time in minutes the patient was in coma before electrostimulation was initiated.

From Traverse City State Hospital, Traverse City, Mich.

BLOOD SUGAR LEVELS In Mg %

Name	Duration of coma	Before Stim.	After Stimulation: Immediately	5 Min.	10 Min.	15 Min.	20 Min.	Comments
D.F.	50'	48	54	60	—	50	43	Lightened*
L.W.	55'	37	45	—	63	—	37	Awake 5' after stimulation
L.W.	50'	23	24	40	68	22	18	Lightened
L.W.	105'	9	20	23	12	7	—	Lightened
L.W.	105'	18	15	23	20	21	—	Lightened
L.W.	115'	27	48	50	44	37	—	Lightened
R.M.	85'	4	12	25	18	9	—	Lightened
R.M.	100'	25	25	34	24	16	—	Lightened
H.B.	110'	7	4	0	4	7	—	Did not lighten
H.B.	110'	25	32	30	15	20	—	Awakened 10' after stimulation. Returned to lightened coma at 15'.
W.B.	75'	19	9	25	16	7	—	Awakened 2' after stimulation
W.B.	75'	44	46	41	40	39	—	Awakened 5' after stimulation

*Return of definite response to pain, voice, and shaking.

Two patients, run as blood sugar level controls with pentothal electrostimulation alone, gave the following results.

BLOOD SUGAR LEVELS In Mg %

Name	Pentothal Dose	Before Stim.	After Stimulation: Immediately	5 Min.	10 Min	15 Min.	20 Min.	Stim. Time	Comments
P.K.	0.4 Gm.	110	120	110	120	104	114	2.5'	Non-fasting
P.K.	0.4 Gm.	63	65	71	77	71	—	1.75'	Fasting
H. O.	0.35 Gm.	128	114	118	110	107	100	3.0'	Non-fasting
H.O.	0.35 Gm.	87	100	94	96	92	—	2.5'	Fasting

*Electrostimulation as in the Hirschfeld technique. (Reiter Electrostimulator.)

As noted in the first chart, two of the five patients treated during insulin coma awakened during one of the trials and one patient awakened on two successive trials. By the term "awakened" we mean that these three patients were fully oriented and coherent and able to take fluids orally, even to the extent of holding their own cups. Similar results were noted in our clinical trials where blood sugars were not done, and in addition the two patients previously noted to have reacted with a grand mal seizure also awakened. Of the three patients who awakened following subconvulsive stimulation one lapsed back into coma in the interval between awakening and having her last blood sugar specimen drawn. This patient's coma, as were those who did not waken, was terminated by intravenous glucose.

In seven of the eight other trials on the insulin coma patients, the patients "lightened." By this we mean that there was a return of their response to pain, voice and shaking. The degree of response in these patients varied but none could be called awake by our criteria.

It is noted that there is some tendency for the blood sugar to show an immediate rise and a later fall in the period following electrostimulation. However, this rise and fall does not occur consistently and, more importantly, does not appear to be significant in regard to whether or not the patient will awaken from coma. The blood sugar levels of the control patients similarly did not appear to vary significantly. While it seems possible that more significant blood sugar changes might be observed by stimulating a larger series of patients yet the positive results in the present rather small series would indicate that patients can awaken without an appreciable rise in blood sugar level. In this regard it was astonishing to observe a patient who was talking rationally and con-

tinuing to do so for ten minutes after the last blood sugar of 7 mgm.% was noted. Although this patient appeared entirely out of coma he was given glucose orally and it was only learned later how low his blood sugar had actually been during the post-stimulation period.

Perusal of the foreign literature subsequent to the initiation of this investigation brought to light the experiences of Riboli with low voltage prolonged administration of alternating current with patients in insulin coma. He reports that an alternating current of 50 to 80 ma. when applied for several minutes would also usually decrease the depth of coma of his insulin patients and frequently waken them. He calls attention to the rise in blood sugar as being the primary cause of the decreased depth of coma; yet he does state that it is a "global excitation of vital neuron complexes of the diencephalon" which, together with the elevated blood sugar, is responsible for the patient's awakening.

Riboli had also observed that patients in prolonged insulin coma who had been given intravenous glucose to the point of hyperglycemia and had not wakened, would be revived from this dangerous state by application of this electrical stimulus. We feel that his observations would make it apparent that the primary factor in the patient's awakening was not the blood sugar level but rather some result of diencephalic stimulation. We believe that our initial observations would suggest that diencephalic stimulation alone is the primary factor in the electrical awakening of insulin coma patients, regardless of whether or not a significant rise in blood sugar level occurred.

Riboli indicated in the same and subsequent articles that his type of low voltage alternating current stimulation would also be useful in wakening patients from deep barbiturate coma. This has also been achieved by Hirschfeld and Robie. It is questioned whether the mechanism involved in wakening these patients is the same one which brought about the wakening of our patients from insulin coma.

The relative unimportance of blood sugar level in regard to the awakening of insulin coma patients is further attested to by Weil-Malherbe in his investigations with glutamic acid injections. He felt that an adrenergic action was responsible for the decreased depth of coma. Whether his method would act to revive the hyperglycemic comatose patient, as reported by Riboli, is open to question. Weil-Malherbe states, "that after the injection or mobilization of adrenalin, auxiliary factors operate which allow the return of consciousness at a lower blood sugar level than after glucose administration." In view of the relatively low blood sugar level at which some of Weil-Malherbe's patients awakened it seems possible that a similar mechanism is at work following both glutamic acid injection and electrostimulation. In Weil-Malherbe's report some patients were noted to be awake at blood sugar levels of 23.5 mgs.% and 30 mgs.%.

Conclusions

1. It is possible to awaken patients temporarily from deep insulin coma by use of prolonged subconvulsive electrostimulation alone, applied bilaterally above the ears with pulsating direct current.

2. This effect is not directly dependent on changes in blood sugar. The lowest blood sugar reading in a case awakened by this method was 7 mgs.%.

3. The convulsive threshold is lower during insulin coma than during sodium pentothal anesthesia.

REFERENCES

Hirschfeld, G. R.: Non-convulsive electro stimulation. A new method of therapy in mental disorders. Presented to New Jersey Neuropsychiatric Association, Lyons V. A. Hospital, Lyons, N. J., Apr. 20, '49.

Riboli, B.: Shock electrico prolungato altre applicazioni delle basse intensita delle comune corrente alternata. (Nota preventiva.) (Prolonged electric shock and other applications of low intensity common alternating current; preliminary report.) *Note e riv. di psichiat.* 74:249-258, Oct.-Dec. '48.

Riboli, B.: Nuovo apparecchio per shockterapie a bassa intensita. (New apparatus for shock therapy of low intensity.) *Note e riv. di psichiat.* 75: Jan.-Mar. '49.

Robie, T. R.: Electrostimulatory therapy as immediate antidote for barbiturate poisoning. Presented to New York Neurological Society, Mar. 14, '50. Abstr.: *Digest Neurol. & Psychiat.,* Inst. of Living. 18:296, May '50.

Weil-Malherbe, H.: The action of glutamic acid in hypoglycemic coma. *J. Ment. Sc.* 95:930-944, Oct. '49.

Unusual Mental Symptoms in a Case of Hepatolenticular Degeneration

W. M. GYSIN, M.D., and EDWIN T. COOKE, M. D.
Fort Lyon, Colorado

Since the original description by Wilson in 1912 of what is now commonly called hepatolenticular degeneration, he and many other authors have seen fit to expand the limits of the concept of the disease. Because of its comparative rarity, each new case is apt to display an additional feature which has not been recorded before, and bring renewed speculation as to the limits of this entity, the probable cause and course of the degeneration, or its significance to psychiatry and neurology.

In 1940 Wilson listed the following criteria for diagnosis: Morphologically, there is a cirrhosis of the liver and degeneration of the lenticular nuclei bilaterally. Etiologically, there is a pronounced familial tendency, as frequently it affects several children in the same family. Usually the disease is first evidenced in the second or third decade and inevitably results in death.

The initial complaint commonly is a motor difficulty of some sort. In the ensuing course the clinical picture is extrapyramidal in nature, manifested by rigidity, dysarthria, tremors, athetoid movements and masking of the facies. Sensation is not disturbed. The liver disease usually is nonsymptomatic. A Kayser-Fleischer ring is found in most cases and is considered a cardinal symptom.

This report brings attention to a case of Wilson's disease which, in addition to most of the typical features, also shows several which have not been described previously.

This twenty-two year old, single, white man was admitted to this hospital in January 1948 from another psychiatric hospital with the diagnosis of schizophrenia. His initial complaints were stiffness of the hands, dysarthria, weakness in his arms, an abnormal gait, occasional drooling, and peculiar mental behavior. Information gathered from the parents, previous hospital records, and the patient revealed the following story:

No history of psychiatric, neurologic or hepatic abnormality could be discovered in the patient's antecedents. The parents were middle-aged, intelligent, moderately successful, but poorly adjusted. They showed a great deal of affection and concern for their son during his illness.

Of the siblings, a younger brother is still living and in good health at the age of eighteen. A younger sister died in 1945 at the age of seventeen. It is important to note that she died of Laennec's cirrhosis. From the first symptoms of vague abdominal pain, she progressed to a picture of advanced portal cirrhosis; death occurred within a month. No neurologic or psychotic symptoms were found in the illness. An autopsy revealed a cirrhotic liver, but no study of the brain was done in compliance with the parents wishes.

The patient enjoyed an average childhood and adolescence, marred only by the fact that he had "malaria" once in his early years. During his school years he received average grades and took part in the usual extracurricular activities. He graduated from high school and shortly thereafter entered the army.

His history during this period with the army is vague and contradictory. It is known, however, that he was assigned as a member of the Military Police, rose to the rank of sergeant, spent fifteen months in the European Theater, and was in combat. According to the patient, he had a severe gastroenteritis, accompanied by hemoptysis, which he thought was caused by "poisoned wine," which necessitated hospitalization for eighteen days. The patient's mother reported that he was lost or absent without official leave for three months after arriving in the United States, but this is not confirmed by army records. There is recorded the possibility that he had three brief psychotic episodes during his service, but for which he was not hospitalized. These were

noted by a friend to have been characterized by confusion, disorientation, incoherency and lack of emotional display.

The patient's first symptom was noted in the service as stiffness and deformity of his hands, with no note of any other physical or mental disability. He was honorably discharged from service in August 1946 with no medical diagnosis or any note of any unusual findings.

Upon his arrival home, both parents were immediately aware that the patient was ill. He was restless, preoccupied, and depressed. He drooled occasionally, had a deformity of the hands and a shuffling gait; and he had difficulty with his speech. At that time he stated that he had felt nervous for the preceding two years and that something was wrong with his digestive system. Also expressed were the ideas that someone was going to kill him, that he was "run down," that he could not sleep, and that he was "no good"; should be shot, and was a coward. A local physician diagnosed his trouble as "battle fatigue," and suggested that he take some training under the "G. I. Bill of Rights."

Subsequently, after a remission in symptoms, he went to school from November 1946 to April 1947. At that time his grandmother died and the patient became briefly psychotic, showing auditory hallucinations, confusion and hyperactivity. He remained at home until November 1947 and then entered the Colorado State Hospital in Pueblo. During this interval he became very forgetful and lost weight. Just previous to his hospitalization, his mother reported that the patient had auditory and visual hallucinations, screamed and shouted in his sleep, felt as if he were losing his mind, and entertained thoughts of suicide. He also carried a gun and threatened his father.

It was reported by the VA Contact Office that during several interviews with the patient, from June 1947 until his hospitalization, he complained of a strong desire to kill people and showed hostility toward his parents. He had a strong guilt feeling over sexual excesses while overseas, and ideas of reference.

Upon admission to the Colorado State Hospital he became violent. He hid under the bed from imaginary pursuers and showed strong paranoid delusions and auditory and visual hallucinations. It was noted there that he had a deformity of his hands—"the metacarpal-phalangeal joints are flexed and the interphalangeal joints extended." His reaction time was increased and blocking was present. Negativism was prominent, and emotionally he showed blunting and depression, expressing ideas of suicide and homicide. Feelings of unreality, confusion, and auditory and visual hallucinations were elicited. His orientation was found to be good, but the sensorium was clouded and thinking capacity was reduced. A diagnosis of schizophrenia, catatonic type, was made and electroshock therapy was administered, with slight benefit.

The initial physical examination at this hospital in January 1948 revealed only moderate malnourishment. The neurological examination showed a gait characterized by stiffness, lack of free swinging motion of the arms, short shuffling steps during which the feet were slapped down, a nasal and dysarthric speech, stooped posture, deformity of the hands with the palms curled and the fingers extended in ulnar deviation, a marked shoulder girdle muscle loss especially on the left, with winging of the scapula, some loss in substance in the arms and hands as compared with the lower limbs, and a flattening of the face. The cranial nerves showed no abnormality except flattening of the right nasolabial fold, the inability of the patient to raise either arm more than ninety degrees, a coarse tremor of the tongue, a weakness in all muscle groups of the hands and arms, as well as a slight weakness in the legs and feet and the muscles of the neck. All deep tendon reflexes were sluggish. Position sense was poor. Finger to nose test showed bilateral ataxia. Adiadokokinesis was present bilaterally and fine movements were severely impaired.

A spinal fluid examination was within normal limits, and the blood and urine revealed nothing unusual. Electrical stimuation of the shoulder muscles pointed toward a partial reaction of degeneration.

Mental examination disclosed a severe psychomotor retardation, with rigidity of

both thought and motor activity. Many bizarre ideas were expressed. Answers to questions were irrelevant and filled with religiosities. The predominant mood was one of depression, and he expressed guilt feelings. Hallucinations were denied. Because of the clouding of the sensorium, bizarre ideation, retardation, emotional inappropriateness and irrelevance, together with the history of delusions and hallucinations, a diagnosis of schizophrenic reaction, hebephrenic type, was made. The neurological condition was considered to constitute amyotrophic lateral sclerosis.

A Wechsler-Bellevue, Rorschach and a Hunt Minnesota were given and the following conclusion drawn:

"Patterning and interpretation suggest a schizophrenic and perhaps also the presence of some sort of organic brain disease or damage to the higher centers.

"Test behavior was interesting. On performance tests the patient showed a fine hand tremor. He sat stiffly in his chair during most of the testing. The pupils were large and there was a flat staring expression. Smiling was childish and often inappropriate and answers were given in a low stilted, almost rhythmical monotone and at times he mispronounced words such as senble for sensible. He drooled now and then and this seemed to embarrass him as he would excuse himself while wiping his mouth. He commented, 'I kind of smell bad, ma'am. I can't help it, I'm kind of sweaty.' Often when the subject could not define a word he would say there was no such word or challenge the examiner to define it. The patient believed the examiner was reading his mind and showed a great deal of negativism and rejection. The Hunt Minnesota test gave a score of 90."

While hospitalized, the patient regained his normal weight and retained it with little variation until the time of his death. He was given a course of electro-shock therapy, with little if any benefit.

As far as his mental symptoms were concerned, the course was exceedingly variable. At times he was surly, negativistic, combative and paranoid, necessitating continuous restraint. At other times he was euphoric, grandiose, delusional and bizarre in his actions and ideas. And, again, he was seclusive, mute, depressed, suicidal and self-condemnatory; but there were flashes of rational behavior, revealing glimpses of an intelligent, personable young man with good insight and judgment. Several trial visits were given, again with variable results. One time he cursed his mother and believed she was poisoning him. He accosted every girl he saw, even when she was accompanied by a man; attacked two young boys with a knife, who he said accused him of being syphilitic; believed himself endowed with superhuman strength and threatened to kill seventeen people who had offended him. On the next trial visit he got along well, was seclusive and content, but had delusions such as Adolf Hitler was on his ward in the hospital. On a later trial visit he tried to kill his mother.

His neurological condition also varied in the degree of incapacity it caused him; but, in general, grew progressively worse. In May 1949 the diagnosis of amyotrophic lateral sclerosis was replaced by undiagnosed disease of the central nervous system.

By June 1949 the patient became bedfast, incoordination was more marked and contractures involved the arms and hands of both extremities, although the right arm could be passively flexed. The facial muscles on the right showed a definite weakness and the face was held in a rigid mask-like manner. Swallowing was done only with extreme difficulty and he had trouble even in inhaling a cigarette. On attempting conjugate deviation, the left eye strayed outward. The winging of the scapulae was more pronounced and movement of the arms was limited to 45° abduction and extension. Both legs were fixed in extension.

Toward the middle of the month he became totally incontinent and terminally was anuric. For the last six days the patient perspired profusely, drank great quantities of water, and began having convulsions varying from 1 second tonic spasm to typical grand mal convulsions, from 3 minutes to 2 to 3 hours apart. On one day, at least 50 convulsive attacks were noted, some starting in the left arm.

The patient did not go into coma until the last few hours of his illness, when he became hyperpyrexic. He died July 7, 1949.

*Pathologic Examination:**

Lungs: Gross—On multiple section, both lower lobes present blotchy, dark cherry red patches. Both lungs are also acutely congested and moderately edematous.

Microscopic—There is irregularly severe hemorrhagic edema.

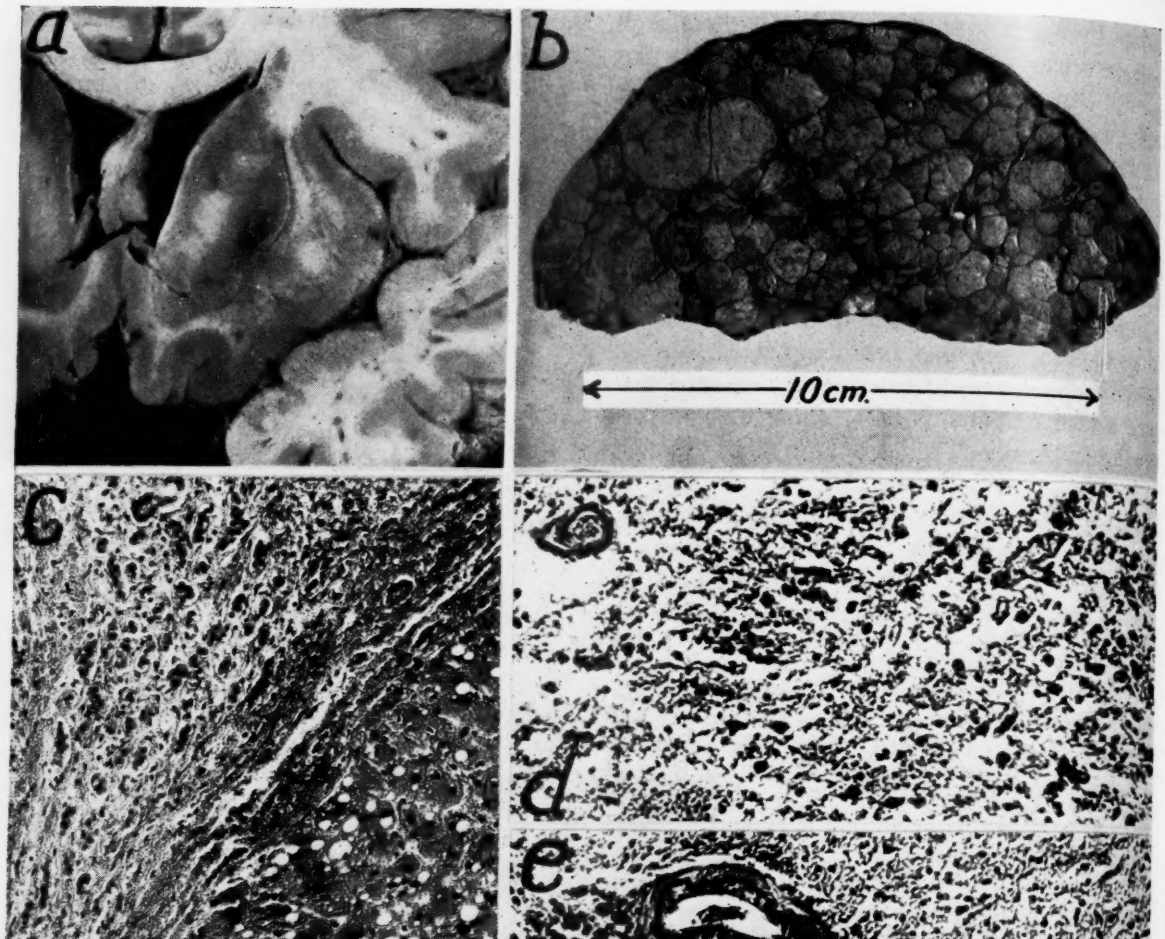

Fig. 1

a. Gross photograph, showing lenticular degeneration (gaseous distention rendered the other half of the brain unsuitable for photography).
b. Cross section of the atrophic, cirrhotic liver.
c. Microphotograph of the liver, showing portal cirrhosis, with fatty metamorphosis.
d. Microphotograph of the lenticular degeneration.
e. Same: encrustation with iron and calcium of a small artery of the globus pallidus.

Aorta and Vessels: The inferior vena cava is dilated two to three times its normal size.

Spleen: Gross—The spleen is noticeably enlarged and weighs 260 grams.

Microscopic—Congestion is marked. There is moderate reticuloendothelial hyperplasia, together with diffuse fibrous thickening of the stroma. The picture is that of moderately severe splenomegaly in portal hypertension.

Liver: Gross—The liver weighs 1610 grams and is obviously involved by a severe cirrhotic process. The capsule is thin and smooth and through it the liver surface is seen to be distorted by innumerable nodules. The size of these nodules or lobules varies from 2 mm to 2 cm and averages 4 to 7 mm in diameter. On multiple section, the liver substance cuts with increased resistance. Approximately half of each cut surface appears to be comprised of circular islands of apparently normal liver tissue, light brown in color, interspersed with circular dirty gray nodules, 2 to 15 mm in diameter, which are slightly firmer than the uninvolved tissue.

Microscopic—Typical and advanced portal cirrhosis is seen. There is marked periportal fibrosis, with supernumerary bile ductules. Hepatic lobules are irregular and there are large, atypical cells, apparently regenerating. Fatty metamorphosis is pronounced. There is no evidence of inflammation.

Brain: Gross—The brain weighs 1400 grams. It appears normal outwardly except for moderate congestion of the leptomeningeal vessels, mild flattening of the convolutions and questionable generalized

convolutional atrophy. Coronal sectioning reveals softening with irregular cavitation of each lenticular nucleus, extending from the medial aspect of each putamen into the medial portion of each globus pallidus. Those portions which are not completely cavitated show slight, pale brown discoloration and friable texture. The subcortical and paraventricular white matter appears to be diffusely gray, especially about the posterior horns of the lateral ventricles. The dentate nuclei show a suggestive blurring of outline.

Microscopic—There is general congestion and the parenchyma appears generally loosened in such a way as to suggest early softening. The myelin appears generally rarefied. Ganglion cells show nonspecific changes of mild to moderate severity, such as swelling or pyknosis. The oligodendrocytes show moderate diffuse proliferation, and there is mild, diffuse gliosis, especially in the white matter. Myelin preparations show the same loosening of the framework, but no active disintegration. The arterioles show mild diffuse hyaline thickening. Sections of the temporal, occipital and parietal regions, and those from the hippocampus, show similar changes, as do sections from the cerebellum and red nucleus. The dentate nucleus is surprisingly well preserved. The cells of the olive show mild fatty changes.

In the lenticular nucleus there is the aforementioned loosening of the tissue. There are swelling and other nonspecific evidences of injury of ganglion cells. Oligodendrocytosis is marked. This is pronounced in the putamen; and toward the inner zone of the putamen and in the globus pallidus complete softening with cavitation has occurred, with influx of fat-filled macrophages. A few atypical, hypertrophied astrocytes are seen. Arteries and arterioles show pronounced ferrugination and calcification, and nerve cells also occasionally are pyknotic and have attracted iron. The arterioles, further, show hyaline degeneration.

In the spinal cord, aside from artefact, only mild changes are seen, resembling those in the cerebral cortex.

Peripheral nerves are not available for study.

Pathological Summary: This is a classic case of progressive hepatolenticular degeneration, with portal cirrhosis of liver, splenomegaly, and encephalopathy, showing the type and distribution which is found in anoxia with involvement of the brain as a whole, including the cerebral cortex, and with characteristic localization of the most severe lesions in the lenticular nuclei.

*Postmortem examination done by Dr. Benjamin S. Wells of this hospital. Gross examination of nervous system and microscopic study of all tissues made by Dr. William B. Dublin, Chief, Laboratory Service, Veterans Administration Hospital, Fort Logan, Colorado.

Summary

1. The case of a patient has been presented in which hepatolenticular degeneration was demonstrated morphologically.

2. As an interesting side-light, a *forme fruste* was noted in a younger sister who died of hepatic disease within a few weeks of the onset of the initial symptoms.

3. A mental disturbance closely resembling a schizophrenic process was noted from the time the patient first came to the attention of psychiatrists, and the diagnosis was continued until the time of his demise.

It is worthy of note because this is the first case, as far as we know that from a review of literature, where the mental aberration in this disease was schizophrenic in nature, although schizoid features have been noted in other diseases with hepatic pathology.

4. The clinical course and symptomatology were, in retrospect, characteristic. The presence of muscular atrophy, as well as the predominance of the schizophrenic features, obscured the proper diagnosis.

BIBLIOGRAPHY

1. Freedberg, H.: Hepatolenticular Degeneration, *Ann. Int. Med.*, 22: 418-425, 1945.
2. Wolaegar, E. E. and Shands, H. C.: Hepatolenticular Degeneration, *Arch. Int. Med.*, 75: 151-154, March 1945.
3. Mowbray, R. and Fidler, H. K.: Degeneration of the Globus Pallidus, *J. Ment. Sc.*, 91: 195-199, April 1945.
4. Rioch, D. M.: Neurophysiology of the Corpus Stratum, *Psychiatry,* Vol. 13: 119-139, February 1940.
5. Bridgeman, O. and Smyth, F. S.: Progressive Lenticular Degeneration, *J. Nerv. and Ment. Dis.,* Vol. 99: 534-543, May 1944.
6. Glazebrooke, A. J.: Wilson's Disease, *Edinburgh Med. J.,* 52: 3-87, February 1945.
7. Wilson, S. A. K.: Neurology, edited by Bruce, A. N., Baltimore, *William Wood and Co.,* 1940, Vol. 2: 806-831.
8. Brinton D.: Wilson's Disease, *Pro. Roy. Soc. Med.,* 40: 556, August 1947.
9. Babcock, C. D. and Brosin, H. W.: Hepatolenticular Degeneration, *Arch. Neurol. and Psych.,* 46: 431-439, September 1941.

Authors' Note: This paper has been reviewed in the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions herein are the result of the authors' own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Neurological Clinical Pathological Conference

of the

Cincinnati General Hospital

CHARLES D. ARING, M.D., *Editor*

Case No. 28822

Presentation

A 52 year old white dog-warden entered the hospital May 22, 1949 because of the sudden onset of paralysis of the lower extremities. On or about May 8 he had contact with a dog thought to have distemper. Shortly thereafter the dog expired and examination of its brain revealed evidence of rabies.

Although the patient had not been bitten or scratched by the dog he was given a series of daily antirabies injections. On May 20, the day of the tenth injection, the patient noted inability to urinate. On the following day he received the eleventh injection. He was catheterized twice on that day because of continued inability to urinate. He complained of constipation. On the morning of May 22 he noticed weakness of the lower extremities when getting out of bed. The weakness soon progressed to paralysis associated at first with aching muscular pain and then with anesthesia.

There had been two previous admissions to the hospital, the first in September 1934 because of traumatic extradural hemorrhage and the second in March 1938 because of post-traumatic personality disorder.

The patient was well developed and nourished. The pupils were round, the right measuring 1.5 mm. and the left 3 mm. in diameter. They reacted equally to light and on convergence. There was slight stiffness of the neck. The parotid glands were moderately swollen and tender. The chest was emphysematous but clear to percussion and auscultation. The heart rhythm was regular. A soft blowing systolic murmur was heard at the apex. The abdomen was distended but not tender. No masses were palpated. Rectal sphincter tone was diminished, and the prostate was not enlarged.

Abnormal neurological signs were generalized muscular weakness in the lower extremities, anesthesia to the level of D8, including loss of appreciation of vibration, but normal appreciation of position of the toes. Deep reflexes were vigorous. Abdominal skin reflexes were absent.

Temperature was 100.2 degrees F, pulse 72 per minute and respirations 22 per minute. Blood pressure was 168/86. Red blood cells numbered 3.53 million; hemoglobin 10 gm.%. The white cell count was 9,900 with 76% neutrophiles. The specific gravity of the urine was 1.007. Microscopic examination revealed 3-10 white cells and 1-5 red cells per high power field. Urine culture yielded B. pyocyaneous, B. proteus and streptococcus fecalis. A blood culture was negative. The blood Kahn test was negative. Blood urea nitrogen was 12 mg.%.

A spinal tap revealed a clear, colorless fluid with an initial pressure of 160 mm. The final pressure was 100 mm. after removal of 12 cc. The fluid contained 331 red blood cells and 232 lymphocytes per c.mm. The total protein was 150 mg.%. The colloidal gold curve was normal. The Wassermann test was recorded as unsatisfactory and was not repeated.

Twelve hours after admission the temperature rose to 103 degrees F, and the level of anesthesia ascended to D5. The patient began to experience respiratory distress. Therapeutic measures initiated at this time included a tracheotomy, Wangenstein suction, tidal drainage of the urinary bladder and intramuscular penicillin. The response was favorable and by the third hospital day the level of anesthesia began to recede. On the 6th day the tracheotomy tube was removed and the Wangenstein suction and penicillin therapy were discontinued. On the 10th day the patient suddenly complained of abdominal pain while sitting on the bed pan. The respirations became rapid and shallow and the pulse imperceptible. Immediately thereafter he became deeply cyanotic, gasped and expired.

Differential Diagnosis

Dr. Albert B. Sabin: This 52 year old man, a dog-warden, was exposed on May 8 to a dog that was believed to have distemper but later it was found to have rabies. The patient had not been bitten or scratched by the dog. As far as I can make out, three days later, on May 11 he had his first inoculation of rabies vaccine and he received a daily injection until May 20. On May 20, after ten injections, he noticed difficulty in urination, let us call it paralysis of the bladder. I cannot make out from the history whether during the preceding days he had headache, fever, nausea, vomiting, or any other prodromal manifestations. It may be a good idea for someone who followed this patient to tell us whether or not there were such symptoms.

Dr. William Ransohoff: No, there were not.

Dr. Sabin: We do not know whether or not the bladder difficulty on May 20 came to the physician's attention. At any rate, he had another inoculation on May 21. Altogether then, there were eleven injections of vaccine.

I'd like to ask another question here. Were the vaccine inoculations given in the abdominal skin?

Dr. Ransohoff: I believe they were given in the arm.

Dr. Sabin: It may be important in trying to interpret the final episode in the life of this patient to know if there might not have been a supply of antigen in the abdominal wall. Usually these inoculations are administered in this region. At any rate we have no certain information on that point in this patient.

On May 22 he had more trouble. The bladder difficulty continued and, in addition, he developed weakness of the legs which precipitated his admission into the hospital. The weakness rapidly progressed to paralysis, associated at first with an aching type of muscular pain and then with anesthesia. The anesthesia, I think, is important and should be underlined.

In his past history we are told of several traumatic episodes in 1934 and 1938, but since his business was with dogs, it would be most important to know whether or not he had previously had rabies vaccine.

Dr. Ransohoff: He had been vaccinated against rabies twice.

Dr. Sabin: When?

Dr. Ransohoff: I believe the first time was approximately 20 years ago and again in 1937.

Dr. Sabin: These are red lights, which should have impressed the person who gave the rabies vaccine to this patient.

Now, what were the other important findings when this man entered on May 22 with paralysis of the legs and anesthesia? We are told that at that time he had a temperature of 100.2 degrees F, that the pupils were unequal, but that they nevertheless reacted normally. There was also slight stiffness of the neck and the parotid glands were recorded as being moderately swollen bilaterally. I find no reference to the parotid glands later on, but we should give this observation consideration. Another thing that is of importance is that the pulse rate was 72; it was neither rapid nor slowed. Another important manifestation in the physical examination here was the confirmation of anesthesia at the level of the 8th dorsal dermatome. It was also significant that vibration was lost but position was intact. The deep reflexes were vigorous and symmetrical. The vigor of the deep reflexes should be correlated with the fact that they were present on the third day after the bladder symptoms first appeared. The laboratory findings were significant only with reference to the lumbar puncture. The fluid was under normal pressure and contained 331 red blood cells and 232 lymphocytes per c. mm. We have no way of telling whether this was a traumatic tap but my impression is that it was not. If it had been, this number of red cells might have been accompanied by one lymphocyte; but there were 232 lymphocytes. Furthermore, the 150 mg. protein cannot be attributed to a traumatic tap.

About twelve hours later the temperature rose to 103 degrees F; the level of anesthsia ascended to D5. The patient began to experience respiratory distress. Therapeutic measures initiated at this time included tracheotomy, tracheal suction, tidal drainage of the urinary bladder and intramuscular penicillin. The response was favorable and on May 24 the level of anesthesia began to recede. On May 27 the tracheotomy tube was removed and suction and penicillin therapy were discontinued. So apparently the patient appeared to be improving 7 to 8 days after the onset of his neurological manifestations.

On May 31, however, we are told that the patient suddenly complained of abdominal pain while sitting on the bed pan. Respirations became rapid and shallow and the pulse imperceptible; immediately thereafter he became deeply cyanotic, gasped and expired.

To summarize, we have here a man who was well up to May 8. He was exposed to a dog with rabies; he was not bitten or injured in any other way by the dog. He had had rabies vaccine in 1929 and in 1937 and again on May 11, 1949. After 10 inoculations, nine days after the first injection, he developed paralysis of the urinary bladder. He received another injection of rabies vaccine, however, and the bladder paralysis became worse. Eleven days after the first dose he had paralysis of the legs, anesthesia and cerebrospinal fluid pleocytosis. After a few days he began to improve but after four days of convalescence he suddenly died.

I made a note of three conditions to be considsidered in the differential diagnosis. First of all, rabies; secondly, poliomyelitis; and finally, postvaccinal encephalomyelopathy. Let us first of all consider rabies. There was nothing about the clinical manifestations which might have excluded rabies. It is rare for rabies to begin in this manner, but such instances were observed in Trinidad many years ago, where rabies was found to be transmitted by the bite of the vampire bat. The bite usually occurred on the big toe, which projected from the bed clothes and was not covered during sleep. These patients showed an ascending paralytic disease which was unlike the classical syndrome of rabies and several years elapsed before the identity of the disease was appreciated.

What is against the diagnosis of rabies? The shortest incubation period on record is 10 days but it is extremely rare for it to be less than 15 days. In this patient it was 12 days. The other thing against rabies is the presence of changes in the cerebrospinal fluid. The vast majority of patients with rabies have no pleocytosis, and in the few who have exhibited it, I believe that the pleocytosis almost never exceeded 100 cells per c. mm. There is so little inflammatory reaction to the rabies virus in the nervous system that the inflammatory cells rarely, if ever, spill over into the subarachnoid fluid. The most important argument against this being rabies is that there was no history of any kind that the virus in the saliva of this dog was introduced into the patient and we have no proven cases on record of rabies without a break in the integument.

What militates against a diagnosis of poliomyelitis? There were no prodromal symptoms, and even more important was the presence of anesthesia and the loss of vibration. This type of sensory involvement is almost unknown in poliomyelitis. Another argument against poliomyelitis was the continued activity of the deep reflexes after so much paralysis had developed. You can get hyperactive reflexes early in poliomyelitis when paralysis of the bladder first appears; you may even see a positive Babinski sign; but it would be most

unusual to have vigorous deep reflexes remaining after paralysis had appeared.

Now we come to post-vaccinal myeloencephalitis. This is the disease from which I believe the patient suffered and I should also like to consider the probable anatomical involvement. The time relationship to the first vaccination 9 days earlier and the succeeding train of paralytic events comprise the classical clinical syndrome of post-rabies vaccine paralysis. As you know, there are known to be at least three possible complications appearing as sequelae to the administration of rabies vaccine. One of them, results from disease of the peripheral nerves and nerve roots, and is perhaps the best kind to have because when recovery occurs it is usually complete. With this type there is usually no cerebrospinal fluid pleocytosis. The second is the "myelitis" type of syndrome, features of which appear to predominate here. With the exception of asymmetry of the pupils, we have very little indication here of involvement of the medulla nor were there evidences of excitement or convulsions to suggest involvement of cortical areas. In the third type there is no paralysis but after preliminary headache and fever convulsions and coma supervene. This is essentially the result of a diffuse lesion of the cerebral cortex.

I think in this patient we have evidence of the second type of syndrome, primarily with diffuse lesions in the spinal cord. Whether the lesions will be found predominantly in the white matter or to some extent also in the gray matter, I can't say. One may be certain, however, that lesions will be found in the tracts of the spinal cord because the manifestations here cannot readily be accounted for on the basis of peripheral nerve involvement. The nerve cells should be intact; the deep reflexes speak for the continuity of the reflex arc. Nor would I anticipate that the cortex was very much involved, although it is possible that certain lesions above the spinal cord may be found to account for the pupillary changes.

Why did this man die four days after he seemed to be getting better? I find nothing in the history to throw light on this. You will recall that I asked whether or not he had received inoculations in his abdomen. He was sitting on a bed pan and I rather suspect that in the process of defecation some massage of the abdomen might have occurred. Since rabies vaccine is a pretty heavy suspension of brain tissue it would not be unusual for considerable amounts of it to remain at the site of inoculation at this late date. It seemed possible that he might have massaged out a certain amount of antigen. As you know, post-rabies vaccine encephalomyelitis, to the best of our present understanding, occurs as the result of some sort of allergic or anaphylactic response to the brain tissue antigen. At least one of the possibilities is that enough antigen was liberated during his exertion on the bed pan to produce anaphylactic shock in a sensitized individual. That there are indeed anaphylactic manifestations in people who get rabies vaccine inoculations is well known. Among those who do not develop central nervous system manifestations there may, nevertheless, occur angioneurotic edema and extensive urticaria.

Why should the fact that this patient had received rabies vaccine in the past have been considered in the nature of a warning? It has been found in the records of neurological complications after rabies vaccine that the incidence is highest in those who had been inoculated before. Sellers[1] of Georgia recently reported that among seven paralytic accidents which occurred among 50,000 people inoculated with rabies vaccine, five had had rabies vaccine before. Frankly, I do not believe that this man should ever have received rabies vaccine on this occasion for he was neither bitten nor scratched by the dog. His history represents one of the contraindications to rabies vaccination. It has been pointed out that "rabiphobia" with consequent unnecessary vaccination is a much more serious problem than hydrophobia.

Dr. Edward Gall: I would like to ask if it is now generally accepted that this disease represents an allergic manifestation?

Dr. Sabin: Many years ago when some of the vaccine used contained live, though fixed, rabies virus there were rare occasions where such manifestations were due to the rabies virus itself. Following inoculation of the noninfective vaccines now in use there has been no evidence that residual rabies virus is itself the cause of this condition. Furthermore, no other viral agent has been recovered. The pathology of rabies vaccine encephalomyelitis is not like that produced by any known virus. Moreover, the pathology and the clinical condition has been reproduced in a large variety of animals simply by inoculating large amounts of brain. For some reason, if you add certain lipid adjuvants to it, particularly extracts of tubercle bacillus, you can, with a single inoculation, produce this syndrome in monkeys and in guinea pigs. Apparently brain substance contains an organ-specific, not a species specific antigen, so that when you inoculate rabbit brain, which is contained in the rabies vaccine, you can produce antibodies against human brain as well as against that of the rabbit and other species. Precisely which antigenic component of brain is responsible for this condition it is not possible to say at this time. There have been encouraging experiments, not as yet confirmed, indicating that it may be possible to extract the vaccine in such a manner as to leave the viral antigen intact and yet remove the antigen which causes the encephalomyelitis in experimental animals.

Dr. M. A. Blankenhorn: Is the time interval after the initial inoculation of such order that you would think sensitization likely?

Dr. Sabin: In people who have not previously had rabies vaccine, the interval of 9 to 10 days after the first dose is not uncommon. However, in a person who has had brain vaccine before, I would not be surprised that even a shorter interval might occur; there are cases on record in which the first neurological manifestations appeared five days after the first dose. I cannot recall now whether this

five-day interval occurred after a primary inoculation or in people who had the vaccine before.

Dr. Ransohoff: I find on reading the chart a note that the right triceps area was red and swollen because of the shots.

Dr. Sabin: I would interpret the record as indicating that the triceps area was used for some of the injections. Whether or not other sites were also used is not clear.

Dr. John Mueller: I'd like to ask Dr. Sabin what he thinks about the parotid glands.

Dr. Sabin: It is remarkable that beyond one note, the record contains nothing more about it. However, when you have parotitis associated with neurological manifestations, one must consider the diagnosis of mumps meningo-encephalitis. I don't think that there has ever been a primary meningitis due to the mumps virus associated with a clinical syndrome like this, but there has been post-mumps encephalomyelities which has stimulated this syndrome. Since I find no further reference to the parotids, I cannot, in my own mind, establish whether or not the parotitis was of the epidemic variety or whether this man happened to have a bacterial parotitis. I can only hope that the pathologist examined the parotid glands.

Dr. William Ashe: Does this type of pleocytosis occur in post-vaccinal encephalomyelitis?

Dr. Sabin: Not only the pleocytosis but red cells too. That is why I was inclined to believe that the red cells were not of traumatic origin. The characteristic lesion one sees in the experimental disease is characterized by a great deal of perivascular red cell extravasation and the cerebrospinal fluid findings are a reflection of such a process.

Pathological Discussion

*Dr. Paul Wozencraft:** If Virchow had performed this autopsy, it is possible that he might have examined the parotid gland. In Virchow's day the delicate art of embalming was not developed and he did not have to worry about undertakers' complaints. The parotids were not examined and were not sufficiently enlarged to call attention to them. The autopsy was performed 72 hours after death. Microscopic examinations of the various viscera did not show any evidence of a virus infection. There was considerable post mortem change and it is important under such circumstances that one should not read anything into the microscopic sections.

The cause of death was a large pulmonary embolus riding across the bifurcation of the main pulmonary artery. There were also evidences of moderate mitral stenosis and an unrelated cystitis. The source of the embolus was not found.

We talk often about pulmonary embolism and we see a good bit of it. The last paragraph of this patient's history has been written countless times in death notes. The patient was sitting on the bed pan, had a sudden chest pain, the breath became short, the patient turned blue, and was very shortly dead. The principle of pulmonary embolism has been established for a long time. We go back to Virchow again, who really promulgated the doctrine. Welch[2] wrote: "Rudolph Virchow is the creator of the doctrine of embolism. There is scarcely another pathological doctrine, of equal magnitude, the establishment of which is so largely the work of a single man. Between the years of 1846 and 1856 Virchow constructed the whole doctrine of embolism upon the basis of anatomical, experimental and clinical investigations, which for completeness, accuracy and just discernment of the truth must always remain a model of scientific research in medicine."

Speculation about thrombosis and embolism had been carried on during this period and before. The paper of Kirkes[3] on embolism from mural thrombi in the heart was published in 1852, but Virchow[4] was really the first man to establish the syndrome of pulmonary embolism as we know it today. The findings that he described in his paper in 1846 have not required much change with time except that we now understand more about the influence of pyogenic and other types of infection, whereas Virchow did not. He made the statement in his paper and printed it in italics that ante mortem clots in the pulmonary arteries were formed either in the right heart or in the veins and were carried along by the circulation. This concept was not at all clear at the time that he published his paper. He came gradually to this conclusion after observing several autopsies.

In one month in the Berlin Charite he found 11 pulmonary thrombi, and again, because he did not need to worry about the undertakers, he was able to find the source in each case. In each instance he was able to find a clot in some other vessel; one was in the iliac vein, 5 were in what he called the crural veins, 3 were in the deep femoral vein, 2 were in the superior longitudinal sinus, and 1 was in the transverse sinus. He pointed out that emboli were found at the divisions of large vessels and sometimes were found riding the bifurcations. He introduced this feature as evidence of the fact that they were true emboli and not thrombi, and he also pointed out that in many instances, the age of the thrombus in the pulmonary artery was the same as that of the peripheral thrombus. He posed several questions that he attempted to answer. One was, "Will thrombi of the size that are found in pulmonary arteries be transported?" Another was, "Will thrombi of higher specific gravity than the blood be carried through the venous circulation?" Another matter that he wondered about was whether or not emboli would go through the heart. He undertook a series of about 35 animal experiments using dogs and these experiments he presented in considerable detail in his paper. He used several substances which he introduced into the veins—usually the jugular vein. He had an extensive source of clots because phlebotomy was a frequent therapeutic procedure in those days, and he used both clotted blood from phlebotomy mate-

*Associate Professor of Pathology.

rial and also from cadavers. He also used pieces of muscle, elder pith, starch particles. The latter he was able to follow and identify again by iodine staining. He also used rubber balls and mercury. Particularly with muscle, when introduced into the jugular vein, he found that embolism would produce sudden death in a dog. The paragraph at the end of our protocol for today is duplicated many times in his clinical protocols and at the end of his paper he gives a detailed account of 12 cases, most of whom died a sudden death, and many of them died sitting on the 19th century counterpart of the modern bed pan. He also mentions swollen legs and bedfast immobility of patients as contributing factors in this clinical condition.

Dr. Murton Shaver: Following fixation, the brain was examined in detail and was found to be generally normal in appearance and aside from general pallor of the tissue suggesting that the body had been embalmed, nothing remarkable was noted. The vessels at the base showed a few atherosclerotic plaques.

Coronal sections through the brain showed slight generalized enlargement of the ventricles while the cut surfaces appeared somewhat wet, but otherwise no remarkable abnormalities were noted.

The leptomeninges of the spinal cord showed generalized congestion of the vessels of the leptomeninges and cerebral tissue with some widening of the perivascular spaces and of the pericellular spaces. No perivascular accumulations of inflammatory cells or red blood cells were seen. In general the cytoarchitecture was well preserved although in patchy areas of the cortex, particularly in the deeper layers, the cells were diminished in number and some of the forms were of ghost type. The cells generally showed moderate degrees of swelling and chromatolysis; some showing more severe degenerative changes and satellitosis appeared with varying frequency. The oligodendroglia generally showed moderate swelling and some increase in numbers, particularly in the white matter. Myelin sheaths were well preserved and showed a slight degree of swelling in some areas. Neurofibrils generally were well preserved.

Sections through the basal ganglia showed moderate generalized congestion of the blood vessels while in the few cases scattered in the perivascular spaces, small aggregations of lymphocytes and plasma cells were observed. A number of the blood vessels showed slight hyperplasia of the endothelial elements, but in general there was no marked increase in cellularity throughout the tissue. The oliogodendroglia appeared swollen in the white matter and slightly increased in numbers. Nerve cells generally showed moderate degrees of swelling matter although some of the myelin sheaths appeared somewhat swollen.

Sections through the upper, middle, and lower pons showed again a generalized congestion of the blood vessels but in increasing gradation; as one progressed down the brain stem there appeared to be more generalized perivascular accumulations of lymphocytes, endothelial, and plasma cells which failed to extend out into the parenchymal tissues. There was no perivascular demyelinization or rarefaction and in general the nerve cells showed only moderate degrees of swelling and chromatolysis. The perivascular accumulations of inflammatory cells were found scattered throughout the tegmentum and in the basis pontis.

Sections through the upper and lower medulla again demonstrated a progressive increase in severity of inflammatory change noted particularly in the perivascular region as one progressed downward through the brain stem. In the upper medullary level, inflammatory cells of monocytic type were found scattered in the perivascular spaces and extended out into the parenchymal tissue for some distance, particularly in the dorsal portions of the medulla.

Dr. Sabin: Dr. Shaver, I wonder if you could show some of those vascular lesions again under higher power. I think the issue here is whether some of these vessels show an actual vasculitis. It is important to know whether the inflammatory reaction involved the walls of the vessels themselves or only the perivascular tissues. I think there is a difference in the pathogenesis of the two types of lesions.

Dr. Shaver: I think that these vessels are too small to make this distinction. We shall see larger vessels in the spinal cord, which may clarify this issue.

In the lower medulla, the extension was still more widespread with marked increase in the numbers of endothelial cells scattered in the surrounding tissue. No definite areas of rarefaction or neurofibrillary degeneration were noted with specific stains. In all cases the inflammatory foci appeared to be located around the blood vessels. The nerve cells in these regions again showed varying degrees of chromatolysis and swelling, and some showed severe degenerative changes with distortion and loss of nuclei and ghost forms. However, some appeared fairly well preserved in areas distant from inflammatory foci.

Sections through the spinal cord demonstrated still more widespread inflammatory foci which became confluent in some areas in the dorsal and lateral columns of the cord. Some of the nerve cells in the anterior horns showed marked chromatolysis and swelling but again some were preserved and showed only slight degrees of swelling. There was no marked diminution in the number of nerve cells noted in these regions. Rarefaction of the tissue in the region of the foci of cellular infiltration was noted particularly in the mid-cervical and more extensively in the thoracic and lumbar region. Here the tissue surrounding the vessels was widely infiltrated with endothelial cells and lymphocytes and irregular areas of demyelinization were seen.

Sections from the above levels of the spinal cord, hippocampus, and pons were stained with specific stains for Negri bodies but none of these bodies were found on careful search.

Clinical Diagnosis

Encephalomyelitis due to rabies vaccine (bulbospinal type).

Pulmonary embolism.

Dr. Sabin's Diagnosis

Post-rabies vaccine encephalomyelitis.

Immediate cause of death unknown, not due to damage in nervous system—possibly systemic anaphylaxis.

Anatomical Diagnosis

Encephalomyelitis due to rabies vaccine (bulbospinal type).

Pulmonary embolism (massive).

Dr. Johnson McGuire: Dr. Sabin, would you explain a bit more fully Seller's observations on paralytic accidents?

Dr. Sabin: There are three sets of data on the incidence of post-rabies accidents. The first goes back over a period of many years to the experiences when dried spinal cord was used. There the incidence reported in 1927 was 1 in 3,000 among 1,164,000 inoculated persons. Some of those might well have been due to rabies itself. With phenolized vaccine, the incidence was 1 in 8,800 in about 500,000 inoculated people. The observations of Sellers in Georgia, using phenolized vaccine was 1 in 7,200 among 50,000 vaccinated people. In addition he reported a selected series of 10,000 patients who were vaccinated not because of a bite, but simply because there was great anxiety resulting from other exposure to rabies. These did not have the 21 inoculations that are usually given, but only 12 injections. None of these 10,000 died of rabies, but 4 developed treatment paralysis with 3 deaths.

Having seen these pathological changes in this patient and knowing the reactions that are produced in monkeys and guinea pigs, particularly monkeys, by inoculating brain, I can say that I personally would have great difficulty in differentiating the two types of reaction but I do want to call attention to a very important difference in the cellular infiltrative changes about the vessels as found here and those which are found in poliomyelitis, viral encephalitis, lymphocytic choriomeningitis and similar viral infections of the nervous system. In poliomyelitis or viral encephalitis, the infiltration appears in the Virchow-Robin space outside the vessel; leukocytes migrate out, but the vessel wall itself does not show any infiltration with cells. There is no evidence of an intrinsic vascular lesion. This sort of perivascular reaction you can get when you have various types of injury to the brain. What struck me in the lesions that Dr. Shaver showed was that many of the vessels showed actual intramural changes which extended directly to the endothelium and appeared like an inflammatory reaction involving the vessel wall itself. It brings to mind some patients with infectious polyneuritis that Dr. Aring and I studied. This is another little understood condition in which some sort of toxic mechanism may be involved. We found many changes in the viscera, particularly in the heart, and the vessels which were affected in the heart also showed this primary vasculitis. Whether or not the basis of post-rabies vaccine encephalomyelitis is a primary attack on the vessels in the brain, it is difficult to say, but certainly the vessels show an inflammatory response. Why the vessels should be picked out in the brain and not the other organs, we don't know. Maybe the other blood vessels and organs might be worth looking at a little more closely, but I think that usually they don't show any such changes.

Dr. Morton Hamburger: Dr. Sabin, what are the indications for the administration of rabies vaccine?

Dr. Sabin: I think that there is a growing body of opinion that believes that rabies vaccination should be restricted to individuals who have definite evidence of injury, a bite or laceration going through the skin, either by an animal proved to be rabid or by an animal suspected of having rabies in which one cannot prove the diagnosis because the animal has run away or his head has been destroyed. On the other hand, where there is no laceration but merely contact with saliva of a rabid animal or the drinking of milk from cows with rabies, I think that in the opinion of many there is greater danger from rabies vaccine than there is from rabies itself.

When there is a history of previous rabies vaccination, one should particularly hesitate to revaccinate unless the indications for this are clear cut. Of course, not all cases fall into the categories that I have given you. The other day somebody called me and said that some children playing on the street were side-swiped by a car and suffered lacerations. A "mad dog" then appeared and one child said that his lacerated hand was inside the mouth of the dog but was not actually bitten. Here there was a fresh laceration and I think I would vaccinate under such a circumstance. But the incidence of such contamination of a fresh wound would be quite low. I think it is generally believed that if there is a fresh laceration, let us say within 24 hours, which has been contaminated with the saliva of a rabid or a suspected rabid dog, it should be regarded as a laceration produced by the rabid animal.

Dr. David Blankenhorn: If you have a patient who you know has been badly bitten by a rabid animal, and on the 8th or 9th day of inoculation he develops a headache, then what do you think is indicated?

Dr. Sabin: Nothing more than a headache?

Dr. D. Blankenhorn: Mild symptoms suggestive of the prodromal symptoms of post-vaccinal encephalitis.

Dr. Sabin: If there are manifestations which are not of allergic (such as urticaria or angioneurotic edema), or paralytic nature, then I think I would continue to give the vaccine. If you have evidence of difficulty in voiding or fever with the headache, I think it would be worthwhile stopping because the danger of a post-vaccinal disturbance is very much greater. A more difficult problem might ensue if

such symptoms appeared while you were vaccinating a patient whose bite was on the face and whose chances of getting rabies were very great. Actually, the chances of the vaccine doing much good in this case would be very slim. There are some situations in which you just have to be a Solomon.

Dr. M. A. Blankenhorn: Is the primary pathology in this disease of vasospastic origin or is it some mysterious chemical interference with the metabolism of the blood vessel wall?

Dr. Sabin: Presumably it is an antigen-antibody reaction across the vessel wall.

Dr. M. A. Blankenhorn: And not mediated by vasospasm?

Dr. Sabin: Vasospasm may be the result of the vasculitis but I doubt if it could cause the vasculitis. Perhaps in a patient exhibiting this sort of syndrome, methods directed at producing vasodilatation might be worth trying.

Dr. Charles D. Aring: What of the report that recently appeared in the PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE that this type of lesion may be prevented in animals by the administration of paraminosalicylic acid?

Dr. Sabin: I saw it, was interested and believe that the work should be repeated.

REFERENCES

1. Sellers, T. F.: Rabies, the Physician's Dilemma. *Am. J. Trop. Med.*, 1948, 28: 453-456.
2. Welch, W. H.: Diseases of the Blood Vessels and Lymphatics. In *Allbutt:* A System of Medicine, Vol. VI. New York, 1900.
3. Kirkes, W. S.: On Some of the Principal Effects Resulting from the Detachment of Fibrinous Deposits from the Interior of the Heart, and Their Mixture with the Circulating Blood. In Willius, F. A. and Keys, T. E.: *Cardiac Classics.* St. Louis, 1941.
4. Virchow, R. Gesammelte Abhandlungen zur Wiessenschaftlichen Medicin. Frankfurt, A.M., Chap. IV, *Thrombose und Embolie,* 1856.
5. Sabin, A. B. and Aring, C. D.: Visceral Lesions in Infectious Polyneuritis. *Am. J. Path.*, 17: 469-482, 1941.

PINEL CLINIC
ELLICOTT CITY, MARYLAND
A Private Sanitarium for the Neuroses and Psychoses
IRVING J. TAYLOR, M.D.
Medical Director
DESCRIPTIVE FOLDER ON REQUEST

Sedation and Euphoria for Nervous, Irritable Patients

VALERIANETS-DISPERT®

Each tablet contains Ext. of Valerian 0.05 gm. dispergentized for maximum efficiency. Odorless and tasteless. Non-habituating. ACTION AND USES: A mild central nervous system depressent. For use in emotional upsets, anxiety states, nervous insomnia, the nervous syndrome of the menopause and of arteriosclerotic subjects.
1 or 2 tablets as required or 3 on retiring. Bottles of 50, 100 & 500.
STANDARD PHARMACEUTICAL CO., INC. 1123 Broadway, New York